

# Air Force Waiver Guide

"This document primarily provides guidance for waivers on trained flying class II and III personnel, and where specifically stated applies to flying class I/IA applicants and other special duty personnel. This waiver guide does not cover general military entrance, commissioning, or enlistment."

Last Update: 14 Apr 2020

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Acne (Apr 2020)

Reviewed: Maj Simon Ritchie (AF dermatologist), Lt Col Jon Ellis (Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** 

New Format, new approved medication (Isotretinoin)

#### I. Waiver Consideration

Per the Medical Standards Directory (MSD), severe acne that is "unresponsive to treatment and interfering with the satisfactory performance of duty or wear of the uniform or use of military equipment" requires an evaluation for retention. Mild to moderate acne in flyers is covered if it is "chronic or of a nature that requires frequent specialty medical care or interferes with the satisfactory performance of military duty" including if it is "severe enough to cause recurrent grounding from flying duties." Treatment with <a href="approved">approved</a> topical agents does not require a waiver for any flying or special duty personnel. The local flight surgeon must confirm, however, there are no adverse effects and the disease itself does not interfere with use of aviation equipment or safe mission completion. Systemic maintenance agents such as oral erythromycin, tetracycline, and trimethoprim-sulfamethoxazole require a waiver for FC I/IA, FC II, FC III, ATC, and SWA personnel. If acne does not interfere with the use of life support equipment, treatment with doxycycline does <a href="maintenance">not</a> require a waiver for any flying or special duty personnel. These oral agents are compatible with flying once it is confirmed that side effects are absent or acceptable in severity.

Isotretinoin therapy may be considered for acne that is refractory to other treatments or causing scarring of the skin. Use of isotretinoin requires a waiver for waiver classes except GBO with a 2-week minimum DNIF period to assess for side effects. Due to the drying effects of isotretinoin on the mucosal surfaces, local flight medicine will need to determine on a case-by-case basis whether this impacts flying duties. Use of isotretinoin in flyers with scanning duties will require a baseline electroretinography (ERG), with a follow up ERG if abnormal.

In addition, waiver will not be considered for acne treated with minocycline. Therapy with oral contraceptives may be considered for women. Isotretinoin therapy requires females of childbearing potential to be on two forms of contraception, one option of which is oral contraceptives. In rare cases, severe nodulocystic acne or scarring may require a categorical waiver to avoid routine use of a helmet or mask.

**Table 1: Waiver potential for acne** 

| Flying Class (FC)         | Acne Treatment  | Waiver Potential                  |
|---------------------------|---|-----------------------------------|
| I/IA<br>II/III<br>ATC/SWA | Topical treatment – topical retinoids (tretinoin, adapalene, tazarotene), benzoyl peroxide, salicylic acid, azelaic acid, topical antibiotics (clindamycin, erythromycin, sulfacetamide-sulfur)             | Waiver Authority <sup>1</sup> N/A |
|                           | Oral contraceptive (female only)  | N/A                               |
|                           | Oral antibiotics - tetracycline, erythromycin, doxycycline, and trimethoprim-sulfamethoxazole. <sup>2,3</sup>   | Yes<br>MAJCOM                     |
|                           | Isotretinoin <sup>4,5</sup>   | Yes<br>MAJCOM                     |
| GBO                       | Topical treatment – topical retinoids<br>(tretinoin, adapalene, tazarotene), benzoyl<br>peroxide, salicylic acid, azelaic acid,<br>topical antibiotics (clindamycin,<br>erythromycin, sulfacetamide-sulfur) | N/A                               |
|                           | Oral contraceptive (female only)  | N/A                               |
|                           | Oral antibiotics - tetracycline, erythromycin, doxycycline, and trimethoprim-sulfamethoxazole. <sup>2,3</sup>   | N/A                               |
|                           | Isotretinoin <sup>4,5</sup>   | Yes<br>MAJCOM                     |

- 1. Waiver authority for untrained applicants is AETC.
- 2. Minocycline is not approved for flying or special duty personnel.
- 3. No waiver is necessary for doxycycline if used for acne.
- 4. Flyers with scanning duties will require a baseline electroretinography (ERG), with a follow up ERG if abnormal.
- 5. Need for ACS case review or evaluation is at the discretion of the waiver authority.

## **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial/Renewal Waiver Request:

- 1. History of acne problem, age at onset of problem, extent and location(s) of lesions, and a description of current and past therapy all medications including dosage, and frequency, and side effects. In adult women, need to address menstrual regularity and presence or absence of hirsutism.
- 2. Comments addressing interference with use of aviation or other military equipment.
- 3. Dermatology consult if individual has recalcitrant moderate to severe inflammatory or severe/nodulocystic acne.
- 4. Medical evaluation board (MEB) reports and narrative if required.
- 5. Isotretinoin use.
  - a. Isotretinoin can only be prescribed by providers who are registered with the iPledge system and are familiar with the medication, its management, and potential side effects. Members require monthly evaluations (typically in person, but can also be accomplished by phone) and can only have 30 days of medicine dispensed to them at a time.
  - b. Standard screening for side effects that may affect duty should be undertaken at the regular monthly visits required for all isotretinoin patients.
  - c. Flyers with scanning duties will also require a baseline electroretinography (ERG) examination.
    - i. If ERG is abnormal at baseline and the member decides to proceed with isotretinoin therapy they will be DNIF throughout the course of therapy (typically 5-7 months) and then will need repeat ERG after therapy is complete demonstrating no significant changes from baseline before consideration of RTFS. This repeat test should be no sooner than 30 days after cessation of treatment with isotretinoin.
    - ii. If ERG is abnormal at baseline (but remainder of vision testing is normal) and member decides to not proceed with isotretinoin therapy, then there is no required DNIF period and local flight medicine in conjunction with ophthalmology will determine need for further workup, if any.
    - iii. If ERG is normal at baseline then waiver can be submitted with the above required information. Member can proceed with isotretinoin therapy and be considered for RTFS after waiver approval and a 2 week DNIF period. Standard screening for side effects that may affect duty should be undertaken at the regular monthly visits required for all isotretinoin patients.
    - iv. ERG can be accomplished either locally (typically only universities will possess this device) or at the aeromedical consultation service (ACS). TDY to ACS for ERG testing will require local funding from the member's unit.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## III. Aeromedical Concerns

Acne is a follicular disease with the principal abnormality being impaction and distention of the pilosebaceous unit. It typically appears at puberty and lessens in severity as adolescence comes

to an end; it is estimated that up to 85% of all adolescents are affected. Although acne is predominately a disease of youngsters in their teens, the mean age at presentation to a physician is 24 years with 10 percent of visits for people between the ages of 35 and 44 years. Recent estimates are that roughly 33 percent of people ages 15 to 44 years are affected by acne. Adolescent acne has a male predominance, but post-adolescent disease predominately affects women. The social, psychological, and emotional impairment that can result from a significant case of acne has been reported to be similar to that associated with epilepsy, asthma, diabetes, and arthritis.

The goals in the treatment of acne are to relieve clinical symptoms and to prevent scarring. As the extent and severity of scarring are associated with the severity and longevity of acne prior to therapy, most dermatologists strongly encourage patients to obtain early treatment. After evaluation of a patient with acne, the patient needs to be given realistic expectations regarding the timeline for improvement. The time for a microcomedo to mature is approximately eight weeks; therefore therapy must be continued beyond eight weeks to assess efficacy. Patients need to receive careful instructions on the proper use of all their medications, as most will be on more than one agent.

The main concerns are interference with the wear of protective aviation equipment; exacerbation of acne due to rubbing, pressure, and/or exposure to hot and humid environments; psychological factors; use of acne medications that are incompatible with flying duties; and extended grounding due to a difficult or prolonged treatment course. Lesions on the face may interfere with mask or respirator seal and helmet wear (chin straps). Lesions on the shoulder, chest, and back may cause discomfort and distraction when wearing restraint or parachute harnesses or with prolonged sitting. Repeated or prolonged rubbing or pressure against the skin can produce or exacerbate an eruption (mechanical acne) with striking inflammation.

Specific to the use of isotretinoin are the known and common side effects of dryness of the mucosal surfaces, photosensitivity, and possible impact on visual acuity. The photosensitizing effects of isotretinoin are moderate, and not usually as significant as that seen with doxycycline (also used in flyers for malaria prophylaxis and acne). The impact on visual acuity, specifically night vision is not well known as there are no studies that specifically evaluate this. However, the potential impact on vision is what drives the need for baseline ERG with possible need for repeat ERG is abnormal at baseline and the member proceeds with therapy. The most common side effect of isotretinoin is the dryness of the skin, but especially of the mucosal membranes. The lips tend to be the most significantly affected surface, but the eyes and nares can also be affected. Any patient on isotretinoin must be evaluated every month by an iPledge provider. Either during this visit, or by a separate visit with flight medicine, it is imperative that the dessicating effect of isotretinoin and its impact on flying duties and wear of aircrew flight equipment is assessed. It is unlikely that these effects would impact flying duty, but nonetheless important to monitor.

AIMWTS review in Feb 2019 revealed 889 Air Force aviators with a diagnosis of acne. There were 75 FC I/IA cases, 357 FC II cases, 2 RPA pilot cases, 359 FC III cases, 72 (ATC/GBC), and 24 MOD. There were 38 disqualifications; 9 were FC I/IA, 4 were FC II, and 20 were FC III, and 4 were ATC/GBC. None of the disqualified cases resulted from the acne diagnosis.

| ICD-9 code for acne |                            |
|---------------------|----------------------------|
| 706.1               | Other acne (acne vulgaris) |

| ICD-10 codes for acne |               |
|-----------------------|---------------|
| L70.0                 | Acne vulgaris |
| L70.8                 | Other acne    |

# IV. Suggested Readings

1. Huang Y, Cheng Y. Isotretinoin treatment for acne and risk of depression: A systematic review and meta-analysis. JAAD June 2017. 76(6):1068-76.

#### WAIVER GUIDE

Updated: May 2014

Supersedes Waiver Guide of Feb 2011

By: Dr Dan Van Syoc

Reviewed by Col Kent McDonald, Chief ACS Neuropsychiatry Branch and Dr. Terry Correll,

ACS staff psychiatrist

## **CONDITION:**

**Adjustment Disorders (May 2014)** 

#### I. Waiver Consideration.

Adjustment disorders that interfere with the safety of flight are disqualifying for all flying classes I/IA, II, III, and for ATC/GBO and SWA personnel. If there are any functional limitations or the adjustment disorder lasts greater than 60 days, a waiver is required. If the DSM-5 diagnostic criteria for adjustment disorder are met, then aviators should be placed DNIF until the disturbance is resolved. If the disorder resolves within 60 days the aviator is placed back on flying status and no waiver is required. If the disorder persists beyond 60 days, or results in hospitalization, the aviator is disqualified and a waiver is required. An evaluation by a qualified mental health professional is required prior to waiver consideration. There is no mandated recovery period before waiver application, except a one-year period after resolution for FC I/IA applicants and other untrained aircrew applicants. The period of remission for trained aircrew should be of such length that the flight surgeon and mental health consultant perceive with confidence that the aviator will not suffer a clinically significant recurrence.

Finally, certain psychiatric disorders render an individual unsuited for duty, rather than unfit, and are subject to administrative separation (IAW AFI 36-3208, para 5.11). Adjustment disorders may fall under this provision if there is unsatisfactory duty performance.

Table 1: Waiver potential for adjustment disorder > 60 days

| Flying Class (FC) | Waiver Potential              |
|-------------------|-------------------------------|
|                   | Waiver Authority <sup>1</sup> |
| I/IA              | Yes <sup>2</sup>              |
|                   | AETC                          |
| II/III            | Yes <sup>2,3</sup>            |
|                   | MAJCOM                        |
| ATC/GBO/SWA       | Maybe <sup>4</sup>            |
|                   | MAJCOM                        |

<sup>1</sup> ACS review or consultation is at the discretion of the waiver authority.

<sup>2</sup> Waiver will not be considered until one-year after resolution for FC I/IA and untrained aircrew.

<sup>3</sup> Waiver is likely if the stressors are resolved, the individual has demonstrated good coping skills, is on no disqualifying medications or is stable on an approved antidepressant, and the adjustment disorder has clearly resolved.

<sup>4</sup> ATC/GBO/SWA personnel with Adjustment Disorder are evaluated based on how the condition affects their ability to continue performing their assigned duties.

AIMWITS search in Apr 2014 revealed a total of 1109 members with an AMS containing the diagnosis of adjustment disorder. There were a total of 492 cases resulting in a disqualification disposition. Breakdown of the cases was as follows: 66 FC I/IA cases (24 disqualified), 220 FC II cases (57 disqualified), 549 FC III cases (246 disqualified), 212 ATC/GBC cases (147 disqualified), and 62 MOD cases (18 disqualified).

## II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

AFI 48-123 –MSD, 13 DEC 2013, Q1 and the Aeromedical Consultation Service (ACS) Waiver Guide addresses waiver evaluations

# Step 1 - Is the aviator ready for waiver submission?

| Step 1 15 the aviation ready 101 warren submissions  |
|--|
| A. Waiver is submitted when 1) the member is asymptomatic and 2)                                       |
| medications/psychotherapy treatment have been completed, as applicable to diagnostic                   |
| category, for the specified time-frame below (Note: psychotherapy "booster sessions",                  |
| and sometimes SSRIs, are permissible and often advisable after initial symptom                         |
| resolution):   |
| 1 Year—Psychotic Disorders & Somatoform Disorders  |
| 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior   |
| Discretion of Flight Surgeon—Adjustment Disorders & V-Codes ("Other Conditions") requiring waiver      |
| For Traumatic Brain Injury cases, please refer to TBI Waiver Guide                                     |
| For aviators with any other psychiatric disorders, please refer to AFI 48-123 and ACS Waiver           |
| Guide  |
| B. To be considered for an aeromedical waiver, any disqualifying condition must meet the               |
| following criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg.31):                        |
|  |
| Not pose a risk of sudden incapacitation   |
| Pose minimal potential for subtle performance decrement, particularly with regard to the higher senses |
| Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment |
| If the possibility of progression or recurrence exists, the first symptoms or signs must               |
| be easily detectable and not pose a risk to the individual or the safety of others                     |
| Cannot require exotic tests, regular invasive procedures, or frequent absences to                      |
| monitor for stability or progression   |
| Must be compatible with the performance of sustained flying operations                                 |
| Step 2 - Before beginning the Aeromedical Summary (AMS), Flight Surgeon must obtain                    |
| Mental Health consultation and ensure it contains items specified below:                               |
| <b>Instructions for the Mental Health Provider</b>   |
| The mental health evaluation must include a <b>comprehensive written report</b> addressing:            |
| Consultation must address each criteria in Step 1B   |
|  |

|          | Clinical mental health history (description of symptoms, treatment modality, frequency and compliance with treatment, relevant personal and family history, and perceived impact on  |
|----------|--|
|          | occupational duties)   |
|          | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)  |
|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)  |
|          | ** for alcohol cases, please comment on carbohydrate-deficient transferrin (CDT) results**   |
|          | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental illness)  |
|          | Current and past aviation related duties and any history of current and past occupational performance difficulties (to include perceived impact of mental health condition on performance of duties)   |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)  |
|          | Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended neuropsychological tests.  Current mental status |
|          | Diagnosis Diagnosis  |
|          |  |
|          | Motivation to fly or engage in special duty operations (past and current)  |
|          | Recommendation for future psychological and medical treatment  |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)   |
|          | Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand for shipment to ACS Neuropsychiatry Branch  |
| Step 3 - | Items for the Flight Surgeon to include in the AMS:  AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safety   |
|          | Summarize Mental Health history and focus on occupational impact   |
|          | ** If 2 or more months have passed since the comprehensive evaluation/report was completed,  |
|          | the flight surgeon should address how the member has done since and consult with the mental  |
|          | health provider if the member has been seen at mental health since the evaluation**  Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)   |
|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)  |
|          | ** for alcohol cases, please comment on carbohydrate-deficient transferrin (CDT) results**  Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if   |
|          | possible - please address current state of any triggers for the mental illness) Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)  |
|          | Current mental status  |
|          | Diagnosis Diagnosis  |
|          | Motivation to fly (past and current)   |
| 1 1      | MOUNTAINOU TO MY (PASE AND CUITCIE)  |

|          | Recommendation for future psychological and medical treatment   |
|----------|---|
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
| Step 4 - | Items to complete the waiver package: Letter of support from command  |
|          | Comprehensive mental health written-report  |
|          | Confirm mental health has made copies of chart(s) and testing. When requested send to:  |
|          | ACS Aerospace Medicine Branch, USAFSAM/FECA<br>c/o Neuropsychiatry Branch<br>2510 Fifth Street Bldg 840<br>Wright Patterson AFB, OH 45433-7913<br>Fax: (937) 904-6296 DSN: 674-9296 |

Please feel free to contact the ACS Neuropsychiatry Branch with questions: SSgt Krista Traut 798-2653, or Mr. John Heaton: 798-2766

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for adjustment disorder should include the following:

A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.

- B. History with special attention to symptoms, frequency, duration, treatment, precipitating factors, action taken to mitigate recurrence and any social, occupational, administrative or legal problems associated with the case.
- C. Copies of psychiatric evaluation and treatment summary (within 3 months of package submission).
- D. Letters from the aviator's squadron commander or operations officer and treating psychiatrist or psychologist supporting or refuting a return to flying status.

The AMS for <u>waiver renewal</u> for adjustment disorder should include the following: A. Interval history and any changes in the aviator's condition with special emphasis on the mental health of the individual.

B. Copies of any applicable evaluations.

#### III. Overview.

Adjustment disorders occur following the development of clinically significant emotional or behavioral symptoms in response to identifiable psychosocial stressor(s). They are categorized by DSM-5 under Trauma- and Stressor-Related Disorders with the stressor(s) typically involving financial struggles, medical illness, and/or a relationship difficulties. These symptoms are diagnostically significant (distinguishing them from ICD-9 V Codes for Occupational Problem, Partner Relational Problem, etc.) if the distress is in excess of what would normally be expected from exposure to the stressor or there is associated impairment in social or occupational functioning. Symptoms associated with bereavement following the death of a loved one are not,

however, classified as an adjustment disorder unless the symptoms are very severe (socially/occupationally impairing) or last longer than expected. At that point, an adjustment disorder or a mood disorder should be considered. An adjustment disorder must begin within three months of the onset of a stressor and resolve within six months of the termination of the stressor or its consequences. Stressors may be a single event, a result of multiple stressors, recurrent or continuous. DSM-IV characterized adjustment disorders lasting longer than 6 months as chronic adjustment disorders; If the disturbance meets the criteria for another Axis I disorder or is an exacerbation of a preexisting Axis I or II disorder, the diagnosis of adjustment disorder should not be utilized.<sup>2</sup> Research indicates the platelet monoamine oxidase activity is lower and plasma cortisol levels higher in patients with adjustment disorder, and suicidality is higher than in gender-matched controls.<sup>3</sup>

## DSM-5 Criteria<sup>3</sup>

- 1. Behavioral or emotional symptoms must develop in response to an identifiable event(s) and occur within three months of the onset of that event(s)/stressor(s).
- 2. These behaviors or symptoms must be clinically significant as evidenced by at least one of the following:
- a. After exposure to the event(s)/stressor(s), the behavioral or emotional symptoms seem in excess of what would be normally expected.
- b. Significant social, occupational, or other functional impairment.
- 3. The disturbance does not meet the criteria for another specific Axis I disorder or is not part of a preexisting Axis I or Axis II disorder.
- 4. The behavioral or emotional symptoms do not represent bereavement.
- 5. Once the event(s)/stressor(s) has terminated, the symptoms do not last more than additional 6 months.

Adjustment disorder is used in psychiatry, but is more typically seen in primary care settings, and has an estimated incidence of 5-21% in psychiatric consultation services for adults. <sup>1, 4, 5</sup> Early interventions with psychotherapy to strengthen coping mechanisms and short-term pharmacotherapy have been shown to promote recovery. <sup>6, 7</sup> Delay in treatment can lead to progression of symptoms to a more severe Axis I diagnosis. <sup>5, 8</sup> Adjustment disorders tend to resolve and only 17-21% ever develop into a chronic course, major depression, or personality disorder. <sup>4, 5, 9</sup> A study in college students noted that a substantial number of students in the first year met adjustment disorder criteria. <sup>10</sup>

There has been little systematic study of adjustment disorder treatment. Psychotherapy is the mainstay of treatment for adjustment disorders. Psychotherapeutic treatment of adjustment disorder enables reduction of the stressor, enhanced coping with the stressor that cannot be reduced or eliminated, and establishment of a support system to maximize adaptation. Psecific treatment interventions include supportive psychological approaches, cognitive-behavioral, and psychodynamic interventions. Short term treatment may be adequate for many individuals; however, more extended treatment may be appropriate in situations in which individual characteristics predispose the individual to stress intolerance. There are very few systematic clinical trials assessing the efficacy of pharmacologic interventions for adjustment disorders. The judicious use of medications to treat specific symptoms associated with adjustment disorders, typically antidepressants and anxiolytics, may be helpful. Surveys of prescribing

habits of office-based physicians show significant increase in prescriptions for antidepressants, particularly SSRIs.<sup>1</sup> Some studies have found SSRIs in the primary care setting are very effective for adjustment disorder with depressed mood.<sup>6</sup>

There is debate in the literature regarding assessment of adjustment disorder with depressed mood and an overlap of Major Depressive Disorder, therefore history and careful diagnosis are very important.<sup>5</sup>

#### IV. Aeromedical Concerns.

Adjustment disorders are one of the most common psychiatric diagnoses among aviators. These disorders are commonly associated with functional impairment resulting from decreased concentration, depression, anxiety, inattention, decreased working/short-term memory, insomnia, fatigue, temporary changes in social relationships and problems with decision making. These impairments are all incompatible with aviation duties.

| ICD-9 codes for Adjustment Disorders |  |  |
|--------------------------------------|--|--|
| 309.0                                | Adjustment disorder with depressed mood                            |  |
| 309.24                               | Adjustment disorder with anxiety                                   |  |
| 309.28                               | Adjustment disorder with mixed anxiety and depressed mood          |  |
| 309.3                                | Adjustment disorder with disturbance of conduct                    |  |
| 309.4                                | Adjustment disorder with mixed disturbance of emotions and conduct |  |
| 309.9                                | Adjustment disorder – unspecified.                                 |  |

| TCD 40      |  |  |  |
|-------------|--|--|--|
| 1CD-10 code | ICD-10 codes for Adjustment Disorders                              |  |  |
| F43.21      | Adjustment disorder with depressed mood                            |  |  |
| F43.22      | Adjustment disorder with anxiety                                   |  |  |
| F43.34      | Adjustment disorder with mixed anxiety and depressed mood          |  |  |
| F43.24      | Adjustment disorder with disturbance of conduct                    |  |  |
| F43.25      | Adjustment disorder with mixed disturbance of emotions and conduct |  |  |
| F43.20      | Adjustment disorder – unspecified.                                 |  |  |

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## WAIVER GUIDE

Updated: Oct 2017

Supersedes Waiver Guide of Oct 2013

By: Aeromedical Consultation Service (ACS) Neuropsychiatry Branch and Dr. Dan Van Syoc

## **CONDITION:**

**Alcohol Use Disorders (Oct 2017)** 

## I. Waiver Consideration.

Alcohol Use Disorders (AUDs), whether mild, moderate, or severe, are disqualifying for all classes of aviation duties in the US Air Force For FC II/III trained assets, these conditions may be waived by MAJCOM/SGPA for a period of no greater than three years. The majority of aviator waiver recommendations for alcohol-related diagnoses are managed through base and command level interaction; Aeromedical Consultation Service (ACS) in-person evaluation is seldom required.

Table 1: Waiver potential for alcohol use disorders.

| Flying Class (FC)       | Waiver Potential <sup>1</sup> Waiver Authority <sup>2</sup> | ACS Review/Evaluation |
|-------------------------|---|-----------------------|
| I/IA                    | Maybe <sup>3</sup>  | Maybe <sup>4</sup>    |
|                         | AETC  |                       |
| II, RPA Pilot, and III, | Maybe <sup>3</sup>  | Maybe <sup>4</sup>    |
| Untrained Assets        | AETC  |                       |
| II/III                  | Yes   | Maybe <sup>4</sup>    |
| ATC/GBO/SWA             | MAJCOM  | -                     |

<sup>1</sup> All aviators with a history of alcohol use disorders must remain abstinent, provide documentation of successful treatment and after-care follow-up, and must not take any medications for substance misuse.

AIMWTS search in Oct 2017 revealed 1240 aviators with a waiver disposition for an alcohol-related diagnosis. There were 32 FCI/IA cases (16 disqualified), 245 FCII cases (57 disqualified), 7 RPA pilot cases (3 disqualified), 667 FCIII cases (280 disqualified), 68 MOD cases (24 disqualified), and 221 cases for GBC/ATC (104 disqualified). Many of the aviators in the pool of 1240 had multiple aeromedical summaries for alcohol-related diagnoses. There were some who were disqualified and later waived, some waived and later disqualified, and a few who were disqualified, waived and then disqualified again.

<sup>2</sup> If there are medical complications from substance use disorders (bleeding varices, cirrhosis, hallucinosis), then an I-RILO is required and the waiver authority becomes AFMRA.

<sup>3</sup> There is no formal waiver provision for UNTRAINED individuals (FC I/IA, FC II/III, or ATC/GBO/SWA). If the waiver authority deems it appropriate, a waiver may be considered on a case by case basis only.

<sup>4</sup> ACS evaluation or review is at the discretion of the waiver authority.

## II. Information Required for Waiver Submission.

## Submitting a Mental Health Waiver Guide:

We encourage all mental health waiver packages to be submitted **30 days BEFORE** the ending of the period of stability to ensure the aviator is evaluated as soon as possible.

Narrative should provide essential information and paint a picture of who this aviator is and his/her capacity and stability in a high stress operational setting.

A well-written and complete waiver package will give the best chance for an ACS aeroletter with no need for a TDY and face-to-face evaluation.

## Required Period of Stability (after reaching "best baseline" functioning)

- 1 Year—Psychotic Disorders, Somatic Symptom and Related Disorders, & Eating Disorders
- 6 Months-Mood Disorders, Anxiety Disorders, PTSD, & Suicidal Behavior
- Discretion of Flight Surgeon—Adjustment Disorders & "Other Conditions" (V & Z-Codes) requiring waiver
- For Traumatic Brain Injury cases, please refer to TBI Waiver Guide
- For aviators with any other psychiatric disorders, please refer to AFI 48-123, Medical Standards Directory (MSD), "Section Q: Psychiatry and Mental Health" and ACS Waiver Guide

The following items are necessary to complete the waiver package. Incomplete packages (including incomplete past mental health records) will prompt a case return, potentially delaying the aviator's return to flight duties.

# 1. Mental Health Evaluation for a Waiver Package

- Uses the Mental Health Template for Narrative (<u>please see template below</u>)
- To be accomplished after "Best Baseline" is achieved and member has demonstrated stability for the time frames listed above.
- The aviator should be evaluated immediately before waiver package submission.
- Mental health evaluations should be performed by a psychiatrist if on medication, or by a psychologist or psychiatrist if not on medication.

## 2. Flight Surgeon's Aeromedical Summary (AMS)

- Utilizes the Flight Surgeon's AMS Template for Mental Health Waivers (<u>please see template below</u>)
- Based on Mental Health Evaluation (#1 above) **and** the flight surgeon's interview of aviator, command, and appropriate collateral sources (supervisor, significant other, etc.).
  - AMS should be written immediately before waiver package submission.

## 3. ALL Past Mental Health and Pertinent Medical Records

Flight medicine staff must make the effort to seek out off-base mental health records. Please ensure <u>both military and civilian provider records</u> are included (mental health records behind "break glass" in AHLTA are needed). Please utilize the attached Release of Information Form (<u>see form below</u>). Search for and include the following <u>as applicable:</u>

- Outpatient, inpatient, partial hospitalization, and intensive outpatient mental health records.
  - ADAPT and Family Advocacy Program notes.

- Any detox or rehab notes.
- Pre-military (i.e., childhood counseling or other prior-service) mental health records, if relevant.
- 4. **Copy of Abstinence Letter**, for alcohol use disorder cases
- 5. Commander's Endorsement Letter

## 6. All Pertinent Labs

- At onset of symptoms
- Current or recent
- Carbohydrate-Deficient Transferrin (CDT), if an alcohol-related case. Need at least two CDT's, unannounced is best, with one ordered at time of waiver package submission.

## **Mental Health Template for Narrative**

- 1. What records were reviewed (military, civilian)?
- 2. Date when symptoms started. Why at that time? Please comment on context and etiology.
- 3. Description of initial symptoms and symptoms at their worst.
- 4. Please describe how symptoms impacted military and flight duties.
- 5. Date, circumstances of presentation, and initial mental health treatment (self-referral, command-directed, sought care after spouse threatened divorce, etc.).
- 6. Type and length of treatment:

Psychotherapy –

- -Who provided (psychologist, social worker)?
- -Type (CBT, PE, etc.), focus, and core issues.
- -Total number of sessions.

Medication therapy -

- -Who provided (psychiatrist, PCM, FS, APN, PA).
- -Medication(s) administered, impact, compliance, side effects, and dates of administration.
- -Current medications.

Healthy lifestyle interventions –

- -Premorbid.
- -Learned and utilized during treatment phase.
- -Current utilization to bolster coping ability and resilience.
- 7. Date aviator returned to "best baseline" even if still receiving ongoing medication(s) or psychotherapy. Please comment on symptom resolution and need for ongoing treatment. Please describe before and after screening or psychological testing, if administered.
- 8. Review of systems, past medical history, past psychiatric history, appropriate developmental, and family psychiatric history.
- 9. Current mental status, level of function at work, in military environment, in family, in personal life, ability to perform under stress and in operational/aviation setting.
- 10. Please comment on awareness, insight, new skills obtained, evidence of their use, coping ability, and successes. Comment on how aviator tolerated past and recent stressors/adversity (indications of resilience).
- 11. Diagnosis, as supported by DSM-5 criteria.

- 12. Estimated risk of recurrence, based on DSM-5, patient's history, and evaluator's experience.
- 13. Motivation to fly.

## Flight Surgeon's AMS Template for Mental Health Waiver

- 1. Date when symptoms started. Why at that time? Please comment on context and etiology.
- 2. Description of initial symptoms and symptoms at their worst.
- 3. Describe how symptoms impacted military and flight duties. FS please make expanded comments here.
- 4. Date, circumstances of presentation, and initial mental health treatment (self-referral, command-directed, sought care after spouse threatened divorce, etc.).
- 5. Type and length of treatment.
- 6. Date aviator returned to "best baseline" even if still receiving ongoing medication(s) or psychotherapy. Please comment on symptom resolution and need for ongoing treatment. FS needs to ensure the appropriate period of stability has been met and should make expanded comments here.
- 7. Current mental status, level of function at work, in military environment, in family, in personal life, ability to perform under stress and in operational/aviation setting. FS should make expanded comments here with specific comments on capability in operational and aviation environment, under stress, etc.
- 8. Please comment on awareness, insight, new skills obtained, evidence of their use, coping ability, and successes. Comment on how aviator tolerated past and recent stressors/adversity (indications of resilience).
- 9. Diagnosis, supported by DSM-5 criteria.
- 10. Estimated risk of recurrence, based on DSM-5, patient's history, and FS's experience.
- 11. Motivation to fly. FS please make expanded comments here specifically addressing ability, stability, and motivation.
- 12. Comments on Command support.
- 13. Estimated aeromedical risk if aviator is returned to flight status. Please address at minimum:
- Risk of sudden incapacitation
- Risk of subtle performance decrement
- Stability under stress (physiologic or emotional)
- Possibility of progression or recurrence
- Need for exotic tests
- Compatibility with the performance of sustained flight operations in austere environments
- 14. FS's endorsement, consultative question(s), and final recommendations.

Narrative should provide essential information and paint a picture of who this aviator is and his/her capacity and stability in a high stress operational setting.

A well-written and complete waiver package will give the best chance for an ACS aeroletter with no need for a TDY and face-to-face evaluation.

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These conditions may be waived by MAJCOM/SGPA for a period no greater than three years. In order to be considered for waiver, three conditions must be met: 1) the individual must have successfully completed treatment (defined below) as determined and documented by the MTF Alcohol & Drug Abuse Prevention & Treatment (ADAPT) program treatment team; 2) the individual must be compliant with post-treatment aftercare program requirements (also defined below) and 3) the individual must have a positive attitude and unqualified acknowledgement of his/her alcohol disorder. Flight surgeon participation in both the ADAPT treatment team meetings and aftercare follow up is required.

Treatment Program Requirements: Individuals will have successfully completed treatment when the following conditions are met: 1) they meet the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for early full remission of substance use disorder; 2) the treatment team determines, based on DSM criteria, the individual shows progress towards agreed-upon goals and/or issues as stated in the treatment plan; and 3) they remain abstinent without the need for AUD medication.

Post-treatment Aftercare Program Requirements: The individual must 1) remain abstinent without the need for AUD medication, 2) document participation in an organized alcohol use aftercare program [e.g., Alcoholics Anonymous (AA), or other program approved by the MTF ADAPT Program Manager], and 3) meet with the designated professionals for the following specific timeframes:

**Table 2: Post-treatment Aftercare Requirements** 

| Professional/Meetings                           | First Year | Second/Third Year | Fourth Year                |
|---|------------|-------------------|----------------------------|
| Flight Surgeon                                  | Monthly    | Quarterly         | Annually                   |
| ADAPT   | Monthly    | Monthly           | N/A                        |
| Psychiatrist, Psychologist, or<br>Social Worker | Annually   | Annually          | N/A                        |
| Organized Alcohol Aftercare<br>Program          | 3x weekly  | 1x weekly         | Recommended (not required) |

#### **Notes:**

- 1. The flight surgeon has primary responsibility for collecting and submitting the required documentation for waiver submission. The ADAPT representative documents alcohol use aftercare program attendance. Temporary modification of aftercare program requirements because of operational demands must be documented by the flight surgeon.
- 2. Initial waiver may be requested after treatment program completion and successful completion of 90 days in the post-treatment aftercare program.
- 3. Unsatisfactory Progress in Aftercare Program: failure of a member to acknowledge his/her alcohol problem, to abstain from alcohol during aftercare, or to comply with all aftercare requirements is medically disqualifying. The following pertain to any individual who fails to remain abstinent or otherwise not comply with all aftercare program requirements: if a relapse occurs during aftercare pending a first waiver, there must be 12 months sobriety / success in aftercare before waiver re-submission. If the member's condition has been waived previously, ground the member and arrange for re-evaluation by flight surgeon and ADAPT provider to determine potential for retreatment. If the member is determined to have potential for retreatment, follow the initial waiver and aftercare program processes. If the member is determined not to have potential for re-treatment, an AMS must be submitted for permanent disqualification. A second waiver request for substance use disorder may be considered in accordance with initial waiver requirements, but requested no sooner than 12 months from the last date that noncompliance with the post-treatment aftercare program was documented. Second waiver requests are considered on a case-by-case basis only, and waiver authority for these individuals is AFMSA/SG3P.
- 4. As part of the waiver package, the individual states in writing that they understand the waiver is valid only if total abstinence from alcohol is maintained, and that a verifiable break in abstinence, once the waiver period has begun, is considered medically disqualifying. This written statement, kept in the medical records, must be accomplished at the initial waiver request, and re-accomplished each time a waiver renewal is requested.
- 5. ACS evaluation is not routinely requested in cases of alcohol use disorders, but such an evaluation may be requested through the MAJCOM if an aviator's flight surgeon and/or commander desire it, particularly for a second opinion. In such cases, a summary of all evaluations (ADAPT Program, medical, and Mental Health) done during the initial workup, a report from a mental health evaluation done within three months of waiver package submission documenting the absence of co-morbid psychiatric pathology and cognitive impairment, an aeromedical summary containing salient laboratory values, and required aftercare documentation should be submitted. Please see mental health waiver submission requirements above.

The AMS for the <u>initial waiver</u> for alcohol use disorders should include the following:

A. Aeromedical summary containing a physical exam and 2 sets of laboratory values (blood alcohol test, urine drug test, CBC with MCV, GGT, SGOT, SGPT, triglycerides, and CDT).

Labs should be collected at treatment initiation and just before waiver submission. Unannounced lab tests are best. The summary should also address work performance, peer relationships,

family and marital relationships, psychosocial stressors, attitude toward recovery, abstinence, AA or other approved alcohol recovery program attendance, and mental status examination.

- B. Copy of alcoholism treatment program summary.
- C. ADAPT statements documenting aftercare and AA or other approved alcohol recovery program attendance.
- D. Copy of annual psychiatrist/psychologist examination while in aftercare.
- E. Letter of recommendation from individual's commanding officer.
- F. Copy of signed abstinence letter (initial and renewal waiver requests must have a signed abstinence statement included as an AIMWTS attachment). In the abstinence letter, the individual states in writing that he or she understands that, if granted, the waiver is valid only if total abstinence from alcohol is maintained. A verifiable break in abstinence once the waiver period has begun is medically disqualifying. The abstinence letter should be signed and dated immediately upon the individual expressing intent to return to flying status.
- G. Medical Evaluation Board report if required.

The AMS for <u>waiver renewal</u> for alcohol use disorder should include the following:

- A. Interval history aeromedical summary since the last waiver.
- B. Flight surgeon summary of any interim alcohol-related treatment to include ADAPT and laboratory results as above drawn at time of AMS.
- C. Consultation from any providers evaluating member for alcohol problems or assessing them for history of same.
- D. Copy of signed abstinence letter (initial and renewal waiver requests must have a signed abstinence statement included as an AIMWTS attachment). In the abstinence letter, the individual states in writing that he or she understands that, if granted, the waiver is valid only if total abstinence from alcohol is maintained. A verifiable break in abstinence once the waiver period has begun is medically disqualifying. The abstinence letter should be signed and dated immediately upon the individual expressing intent to return to flying status.

#### III. Overview.

Excessive alcohol consumption can significantly impair social, interpersonal, and/or occupational functioning. These disorders commonly develop between the ages of 20 and 40. AUDs in the U.S. military are well described public health problems. Given the accessibility of alcohol and its common use in military culture, service members may use alcohol consumption as a recreational activity or to help cope with stressful or traumatic events associated with military duties or combat. Several studies demonstrate that military members are involved in heavy drinking (five or more beverages on occasion within the last two weeks) twice as often as compared to similarly matched civilian populations. From 2001-2010, there was a sharp increase in the use of alcohol among all U.S. military branches. More than one-fifth (21%) of all acute alcohol-related encounters were recurrent diagnoses and the proportion of recurrences was higher among those in combat occupations (26%). Along with alcohol misuse, abuse and dependence (DSM-IV-TR criteria) are among the most commonly seen psychiatric issues encountered in aerospace medicine. Recent diagnostic changes per DSM-5 no longer differentiate between alcohol abuse and alcohol dependence. Studies revealed little functional difference between the disorders and the new manual, therefore, classifies AUDs along a spectrum from unaffected, mild, moderate, to severe. The new diagnostic criteria are a

combination of the old from alcohol abuse and dependence adding "craving or a strong desire or urge to drink" as a new criterion and dropping "recurrent legal problems" due to poor discrimination ability. By DSM-5 AUD criteria, those endorsing 0-1 criterion (out of a total of 11) would be classified as unaffected, those endorsing 2-3 criteria would have a diagnosis of mild AUD, 4-5 criteria would have a diagnosis of moderate AUD, while endorsement of 6+ criteria would indicate severe AUD. As with all DSM-5 diagnoses, sound clinical judgment is required in establishing the correct diagnosis.

Ranked the third leading cause of preventable death in the United States, alcohol use results in approximately 75,000 fatalities annually and is associated with liver disease, cardiomyopathy/arrhythmias, gastritis, mental disorders, motor-vehicle fatalities, suicide and decreased/poor job performance. Operational effectiveness in the USAF can be seriously hampered as a result of AUDs. Many flight surgeons would agree that alcohol problems are the "number one killer" of aviator careers.

AUDs can be difficult to detect. Secondary to expected minimizing and even frank denial of alcohol use, there is not one objective parameter that can be used to make the diagnosis. Therefore, a flight surgeon must be aware and watchful of circumstances which can signal their presence, (e.g., alcohol on the breath during duty hours, an alcohol-related incident, such as a DUI or domestic incident, an elevated blood alcohol level above 100 mg/dL (0.10%) in a person not appearing drunk, unexplained insomnia or hypertension, vague GI problems, frequent minor injuries, along with "broad spectrum" dysfunction in the member's life). Laboratory abnormalities such as elevations of MCV, GGT, ALT, AST, uric acid, triglycerides, or increased carbohydrate deficient transferrin (CDT) may also be present. A CDT greater than 3% indicates the regular intake of 4-5 standard alcoholic beverages for several weeks prior to the test, especially revealing in aviators who have signed abstinence agreements. The CDT specificity is over 95% for excessive alcohol use with false positives found primarily in significant hepatic disease.

Chronic depression, irritability, and anxiety may indicate the presence of an AUD, especially when they represent a change from a flyer's normal personality. Alcohol use often causes light, broken sleep due to sympathetic arousals throughout the sleep cycles. Screening questionnaires (CAGE, MAST, SASSI, AUDIT, and McAndrew) are available for use by the flight surgeon or through the Mental Health Clinic. Recently, the National Institute of Alcohol Abuse and Alcoholism has developed a single-question test for primary care doctors to replace longer questionnaires. This question asks, "How many times in the past year have you had (for men) 5 or more drinks or (for women) 4 or more drinks in a single day?" Answering "1 or more days" in the past year should prompt further investigation. Screeners cannot make or confirm the diagnosis, but they can help inform the clinician to further evaluate for the presence, extent, and severity of alcohol use problems. Clinical correlation with focused interviews and reaching out to collateral contacts are helpful. Sound clinical judgment is required.

Per AFI 44-121, it is the responsibility of the flight surgeon to inform the commander and notify the Alcohol & Drug Abuse Prevention & Treatment (ADAPT) program manager of an individual who has been admitted for alcohol detoxification, receives treatment for an injury or illness that may be the result of substance use, or is suspicious of having an alcohol problem. Referral and

enrollment in the ADAPT program is key to starting the member on the correct path. Along with the usual medical evaluation, the workup should include an assessment for other psychiatric disorders, such as major depressive disorder, anxiety disorders, and personality disorders, for which those with AUDs are at increased risk.

A recent study showed that relapse rates among Air Force personnel are as high as 35%. Abstinence from alcohol is the preferred modality for preventing relapse in aviators. Abstinence has been associated with a lower risk for relapse when compared to low risk, so-called "controlled," drinking. Some studies have shown that limited drinkers were four times more likely to relapse to unacceptable drinking levels than were those who reported total abstinence.

## IV. Aeromedical Concerns.

A continuum exists ranging from normal social use of alcohol to full-blown AUDs. As an alcohol problem progresses, it often causes problems at home first, then in the social environment. Performance in the cockpit may be the last area to be affected. One of the more vital roles of the flight surgeon is involvement with the squadron aircrew in their off-duty time and, in particular, participation in social and recreational activities where the use of alcohol often occurs. If an aviator is willing to drink excessively in front of supervisors or commanders, that should raise serious concerns.

Alcohol misuse presents hazards to aviation because of both acute and chronic effects on cognitive and physical performance. Acute alcohol intoxication and hangover are obviously incompatible with flying. Similarly, alcohol withdrawal is a threat to flight safety due to anxiety, tremor, and the possibility of arrhythmia or seizure. Further, subtle cognitive impairment, manifesting as slowed reaction time, inattentiveness, difficulty in monitoring multiple sensory inputs, and difficulty making rapid shifts of attention from one stimulus to another, can occur after low doses of alcohol which would not cause intoxication. After moderate alcohol consumption, impairments can persist for many hours after the blood alcohol level has returned to zero, well beyond the 12-hour "bottle-to-throttle" guidelines. Positional alcohol nystagmus, indicating impairment in vestibular function, can occur under G-load up to 48 hours after alcohol consumption. Heavy drinkers are at risk for arrhythmias ("holiday heart") for several days after drinking. Post alcohol impairment ("hangover") causes well-known difficulties such as headache, fatigue, nausea, anorexia, anxiety, irritability, diaphoresis, and thirst, but also impaired "higher" cognitive functions for as long as 72 hours later. Therefore, due to the many known repercussions from even "normal" use of alcohol, aviators would optimally be informed to be abstinent for at least three days prior to flying.

| ICD 9 codes for alcohol abuse and dependence (no current ICD-9 code for alcohol use disorder) |                    |  |
|---|--------------------|--|
| 305   | Alcohol Abuse      |  |
| 303.9   | Alcohol Dependence |  |
| -   |                    |  |

| ICD 10 codes for alcohol abuse and dependence |                    |  |
|---|--------------------|--|
| F10.10  | Alcohol Abuse      |  |
| F10.20  | Alcohol Dependence |  |

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| AUTHORIZATION FOR DISCLOSURE OF MEDICAL OR DENTAL INFORMATION   |                                    |                                    |  |
|---|------------------------------------|------------------------------------|--|
| PRIVACY ACT STATEMENT   |                                    |                                    |  |
| In accordance with the Privacy Act of 1974 (Public Law 93-579), the notice informs you of the purpose of the fo |                                    |                                    |  |
| and ho w it will be used. Please read it carefully.   | <i>,</i>                           | 1 1                                |  |
| <b>AUTHORITY:</b> Public Law 104 -191; E.O. 9397 (SSAN)   | ; DoD 6025.18 -R.                  |                                    |  |
| <b>PRINCIPAL PURPOSE(S):</b> This form is to provide the  | *                                  | ental Treatment                    |  |
| Facility/TRICARE Health Plan with a means to request the  | •                                  |                                    |  |
| information.  |                                    | 1                                  |  |
| <b>ROUTINE USE(S):</b> To any third party or the individual u   | upon authorization for the disc    | losure from the individu           |  |
| for: personal use; insurance; continued medical care; school  |                                    |                                    |  |
| <b>DISCLOSURE:</b> Voluntary. Failure to sign the authorizat  |                                    |                                    |  |
| SECTION I - PATIENT DATA  |                                    |                                    |  |
| 1. NAME (Last, First, Middle Initial)   | 2. DATE OF BIRTH                   | 3. SOCIAL SECURIT                  |  |
|   |                                    | NUMRER                             |  |
| 4. PERIOD OF TREATMENT: FROM - TO   | 5. TYPE OF TREATMEN                |                                    |  |
| (YYYYMMDD)  | OUTPATIEN INPAT                    | IENT BOTH                          |  |
| SECTION II - DISCLOSURE<br>6. I AUTHORIZE   | T                                  | O RELEASE MY PAT                   |  |
| INFORMATION TO:   |                                    | ) KELEASE WII I AII                |  |
| a. NAME OF PHYSICIAN, FACILITY, OR  | <b>b. ADDRESS</b> (Street, City, S | State and ZIP Code)                |  |
| TRICARE HEALTH PLAN   | 2510 5th Street, Bldg 840, A       | ,                                  |  |
| c. TELEPHONE (Include Area Code) (937) 938-2768   | d. FAX (Include Area Code          | ) (937) 904-8753                   |  |
| 7. REASON FOR REQUEST/USE OF MEDICAL INF  |                                    |                                    |  |
| PERSONAL USE CONTINUED X  | OTHER (Specify) ACS WA             | IVER PACKAGE                       |  |
| INSURANCE MEDICAL CARE  | SCHOOL                             |                                    |  |
| 8. INFORMATION TO BE RELEASED   |                                    |                                    |  |
| All Mental/Behavioral Health (Sections A-F), ADAPT, FA  | AP, and/or civilian records (wh    | en applicable). Please in          |  |
| any and all of the records to include, but not limited to: bac  | ekground questionnaires, intak     | e forms,                           |  |
|   | IZATION EXPIRATION                 |                                    |  |
|   | YYMMDD)                            | ACTION COMPLE                      |  |
| SECTION III - RELEASE AUTHORIZATION   |                                    |                                    |  |
| I understand that:  |                                    |                                    |  |
| I have the right to revoke this authorization at any time. N  | •                                  | 0 1                                |  |
| where my medical records are kept or to the TMA Privacy   |                                    | *                                  |  |
| by the TRICARE Health Plan rather than an MTF or DTF.   |                                    |                                    |  |
| person(s) I herein name will have used and/or disclosed my  |                                    |                                    |  |
| If I authorize my protected health information to be disclo   | _                                  |                                    |  |
| privacy protection regulations, then such information may   |                                    |                                    |  |
| I have a right to inspect and receive a copy of my own pro  |                                    |                                    |  |
| accordance with the requirements of the federal privacy pr  | rotection regulations found in     | the Privacy Act and 45 (           |  |
| 11. SIGNATURE OF PATIENT/PARENT/LEGAL   | 12. RELATIONSHIP TO                | 13. DATE (YYYYMMD)                 |  |
| REPRESENTATIVE  | PATIENT                            | (                                  |  |
| SECTION IV - FOR STAFF USE ONLY (To be comple   | ted only upon receipt of writte    | n revocation)                      |  |
| 14. X IF 15. REVOCATION COMPLET   |                                    | <b>16. DATE</b> ( <i>YYYYMMD</i> ) |  |
| AUTHORIZATIO  |                                    | ,                                  |  |
| N REVOKED   |                                    |                                    |  |

17. IMPRINT OF PATIENT IDENTIFICATION PLATE WHEN AVAILABLE

SPONSOR NAME: SPONSOR RANK: FMP/SPONSOR SSN: BRANCH OF SERVICE: PHONE NUMBER:

## WAIVER GUIDE

Updated: Jun 2017

Supersedes Waiver Guide of Jul 2013

By: Dr Dan Van Syoc

Reviewed by Lt Col Christopher Coop, allergy consultant to AF/SG

## **CONDITION:**

Allergic Rhinoconjunctivitis (Jun 2017)

#### I. Waiver Consideration.

Historically, the waiver approval rate for allergic rhinitis has exceeded 99%. The AFMOA Policy Letter, "Nasal Steroids and Nasal Cromolyn Sodium Use in Aviators", dated May 2001, approved the use of topical nasal steroids or cromolyn for the treatment of mild allergic, non-allergic or vasomotor rhinitis without a waiver. The length of DNIF is dictated by the time required for control of underlying symptoms. In July 2004, the HQ USAF/SGOP Policy Letter, "Medication Changes for Aviators and Special Duty Personnel", approved the use of loratadine (Claritin®) or fexofenadine (Allegra®) for the treatment of mild allergic rhinitis without a waiver. A minimum of 72 hours as a ground trial at initiation of therapy to ensure adequate symptom control and to exclude idiosyncratic reactions is required. Loratadine is limited to a maximum dosage of 10 mg per day. As an aside, the combination therapy of azelastine with fluticasone has proven more beneficial than fluticasone alone in moderate to severe cases. Refer to the Official Air Force Aerospace Medicine Approved Medications list for any specific medication questions.

According to AF policy, a waiver is required for FCI/IA, II, III, and SWA duties for AR unless it is mild in degree, controlled on approved medications and unlikely to limit duty. For seasonal cases only requiring approved antihistamines, montelukast, or nasal steroids, a waiver is not required. A waiver for medical therapy is necessary for the use of immunotherapy (desensitization) and azelastine, and these will not be indefinite. For ATC duties, symptomatic AR not controlled by use of a single approved medication is disqualifying. It is not listed as disqualifying for GBO duties or for retention purposes.

A verified history of allergic, non-allergic and vasomotor rhinitis after age 12, unless symptoms are mild and controlled by a single approved medication, is disqualifying for FC I/IA. Therefore, a waiver is required for FC I and IA duties for AR successfully treated with <u>more than one</u> of the following: an approved second-generation antihistamines, topical medications, montelukast or immunotherapy.

The use of Claritin-D® or Allegra-D® is not approved for flying duties.

**Table 1: Waiver potential for allergic rhinoconjunctivitis** 

| <b>Flying Class</b>  | Condition          | Waiver Potential | ACS Evaluation or |
|----------------------|--------------------|------------------|-------------------|
| (FC)                 |                    | Waiver Authority | Review            |
| I/IA*#               | AR                 | Yes α            | At the request of |
|                      |                    |                  | AETC              |
|                      |                    | AETC             |                   |
| $\Pi^{*\#}$          | AR                 | Yes              | At the request of |
| $\mathrm{III}^{*\#}$ | (more than mild or | MAJCOM†          | MAJCOM            |
|                      | not controlled by  |                  |                   |
|                      | approved           |                  |                   |
|                      | medications)       |                  |                   |
| ATC*#                | Symptomatic AR     | Yes              | No                |
| SWA*#                | (more than mild or | MAJCOM†          |                   |
|                      | not controlled by  |                  |                   |
|                      | approved           |                  |                   |
|                      | medications)       |                  |                   |
| GBO                  | AR                 | N/A              | N/A               |

 $<sup>\</sup>alpha$  No requirement for FCI/IA waiver for AR or history of same after age 12, if symptoms are mild and controlled on a single approved medication.

A review of AIMWTS in Jun 2017 revealed 4695 submitted cases with a history of AR. There were 687 IFC I/IA cases, 2141 FC II cases, 10 RPA pilot cases, 1532 FC III cases, 278 ATC/GBC cases, and 47 MOD cases. There were a total of 323 disqualifications. The vast majority of the disqualified cases were due to causes other than the allergic rhinitis diagnosis.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

AMS for <u>initial waiver</u> for AR should include the following:

- A. History of symptoms: dates, treatments (to include any possible skin testing and allergy shots) and effect of symptoms on everyday life and job.
- B. Physical examination with emphasis on ears, nose, eyes, pharynx and lungs.
- C. Use of an approved treatment.
  - immunotherapy (waiver required for FC I, IA, II, III and SWA)
  - azelastine (waiver required for FC I/IA, II, III and ATC; for FCII waivers, AFMRA may require a FCIIC)
- D. Consultation report from allergy provider. If the history is remote (no symptoms for at least one year), it is reasonable to only require a good synopsis of the problem.
- E. Documentation that symptoms greatly improved or resolved on therapy and that there are no side effects from therapy. AMS for <u>waiver renewal</u> for allergic rhinitis should include the following:

<sup>\*</sup>All medication usage must be in accordance with the most recent Air Force Approved Aircrew Medications list. # Indefinite waiver appropriate for all cases except those requiring immunotherapy.

<sup>†</sup>Waiver authority for medication not on the Approved Aircrew Medication List is AFMRA.

- A. Interval history since last waiver submittal; document impact of AR on everyday life and job.
- B. Physical examination as above
- C. Consultation report from allergy provider.

#### III. Overview.

Allergic rhinoconjunctivitis (AR) is usually considered a relatively minor health condition. However, it can result in major adverse effects in aviators in light of the unique environmental and physical stresses of flight. The prevalence of AR has been noted to be rising in developed countries leading allergists to speculate that environmental factors may be more important that genetic influences.<sup>4</sup> AR is the most common of allergic disorders, affecting an estimated 20 to 40 million people in the United States and up to 30% of adults worldwide.<sup>5, 6</sup> For the average person, AR is a nuisance; for aircrew it can be a serious and potentially fatal condition. Aircrew can be adversely affected by AR because the condition can diminish active flying operations and readiness through temporary flying duty restrictions. 7-9 One study at a US Coast Guard air station found 5.7% of total days restricted attributed to allergic causes (allergic rhinitis and asthma). 10 Currently, the modes of therapy acceptable for flying duty (intranasal steroids and mast-cell stabilizers, some second-generation antihistamines, leukotriene modifier [montelukast] and immunotherapy) are generally effective. However, the actual impact of AR on mission effectiveness in terms of temporary flying duty restriction is unknown. AR has been shown to increase health care utilization and health care expenditures in relation to patients who do not have AR.11

AR often occurs seasonally in direct response to elevated airborne pollens but can also exist perennially (such as house dust mites, pet dander, cockroaches and some molds). A family history of allergies is often present. The symptoms of common "hay fever" include nasal pruritus, congestion, rhinorrhea, sneezing, eye irritation, pruritus, and olfactory dysfunction. Clinical findings include edematous or inflamed nasal mucosa, increased nasal secretion (which is typically clear), and conjunctival edema and erythema. Difficult cases may require skin or serologic tests to allergens. However, in most cases the appropriate diagnosis can be made on the basis of a careful medical history, thorough clinical exam, and a documented response to appropriate therapeutic intervention. The differential diagnosis includes viral upper respiratory infection (URI), non-allergic rhinitis, sinusitis and side effects of medications. Abuse of decongestant nasal sprays (rhinitis medicamentosa) and anatomic deformity should also be excluded as a cause of chronic congestion and obstruction. For cases of prolonged or moderate to severe symptoms a formal allergy consultation may be appropriate. Anatomic causes for chronic rhinitis can most easily be ruled out via sinus CT and/or rhinoscopy.

The mechanisms for upper airway allergic reactions is complex and involves allergen-specific immunoglobulin (IgE), mast cells, basophils, environmental influences, and a host of other immunologic reactions. There can be immediate and late nasal reactions, and inflammatory changes within the lining of paranasal sinuses is common.<sup>13</sup> For people with AR, there is a significant increase in the probability of asthma. Some studies have shown that up to 40% of those with AR have or will have asthma symptoms.<sup>14</sup>

Topical drug therapy for mild to moderate symptoms of AR consists of intranasal delivery of topical steroids or nasal antihistamine sprays such as azelastine (Astepro® or Astelin®) and olopatadine (Patanase®); only olopatadine is currently approved for use by aircrew. The steroids act as local anti-inflammatory agents and the antihistamines work locally. These agents are very effective but may take several days to reach the desired effect. Intranasal steroids are widely accepted as the most effective and preferred first-line treatment for AR. Oral antihistamines are another choice for acute and chronic control of allergic rhinitis. Antihistamines competitively inhibit binding of histamine to H<sub>1</sub> receptors. Fexofenadine (Allegra®), or loratadine (Claritin®) (10 mg dose only) are the only aeromedically approved second-generation antihistamines. Because these medications are larger molecules they do not cross the blood-brain barrier and are considered non-sedating antihistamines. Loratadine at doses higher than 10 mg per day can cross the blood-brain barrier and is therefore not approved at these doses for use in USAF aviators. Montelukast (Singulair®) has shown modest control of allergic rhinitis and is an overall safe drug (do beware of the black box warning for Singulair® regarding neuropsychiatric effects such as agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behavior, and tremor) and oral decongestants such as pseudoephedrine can be utilized as well. If a patient responds poorly to nasal spray, antihistamines or montelukast, immunotherapy may then be considered. Immunotherapy carries a higher risk of serious adverse reaction and the initiation and maintenance of treatment are more complicated than with nasal spray or antihistamine. <sup>15-17</sup> A treatment course in immunotherapy typically lasts 3-5 years. There has been increased interest in the use of sublingual immunotherapy for the treatment of AR. Although there are no reported life-threatening adverse effects, the jury is still out on whether this is an effective therapy for those suffering with AR. 18-20

Finally, there are some newer therapeutic options available for the more difficult cases. Immunomodulatory treatments and antibody treatments may be used for such patients, but their use would not be approved for aviators. <sup>18</sup>

## II. Aeromedical Concerns.

Potential hazards include: ear and sinus barotrauma with potential in-flight incapacitation; airway compromise; discomfort and distraction; reduced sense of smell; and possible use of easily accessible, unauthorized over the counter medication. Symptomatic allergies with sneezing could be a particular hazard in high speed, low level flight. Barotrauma as well as infectious complications can lead to prolonged periods of flying restriction, reducing operational effectiveness and mission effectiveness.

Antihistamines may adversely influence cognition and performance; hence, ground testing prior to acceptance for operational use is required.<sup>22</sup> It is important to note that antihistamines and topical steroids do not significantly improve the sense of smell, therefore symptomatic relief needs to consider olfactory function.<sup>23</sup> Idiosyncratic reactions need to be excluded for any selected mode of therapy. Additionally, symptomatic control should be achieved. Because of the risk of an allergic reaction to an immunotherapy injection, the flyer should remain in the physician's office for approximately 30 minutes post-injection. DNIF is required until potential idiosyncratic reaction is ruled out and adequate control is maintained before submission for a

waiver. Once a waiver has been granted (when maintenance dosage reached or symptoms under control) a 4-hour verbal DNIF is required for aircrew after each injection. DNIF is not required for ground operations. Aircrew will not deploy on immunotherapy.

|                         | DNIF Duration  |
|-------------------------|--|
|                         | Rule out idiosyncratic reaction and ensure all symptoms are resolved |
| Claritin                | Minimum 72 hours   |
| Allegra                 | Minimum 72 hours   |
| Nasal Steroids          | Time required for symptom control                                    |
| Nasal<br>Antihistamines | Time required for symptom control                                    |
| Oral<br>Decongestants   | Time required for symptom control                                    |
| Cromolyn Sodium         | Time required for symptom control                                    |
| Montelukast             | Time required for symptom control                                    |
| Immunotherapy           | Symptom control and 4hr verbal DNIF after each injection             |

| ICD 9 code for Allergic Rhinoconjunctivitis |                   |  |
|---|-------------------|--|
| 477   | Allergic Rhinitis |  |

| ICD 10 code for Allergic Rhinoconjunctivitis |                                |  |
|--|--------------------------------|--|
| J30.9  | Allergic Rhinitis, unspecified |  |

## V. References.

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#### WAIVER GUIDE

Updated: Mar 2016

Supersedes Waiver Guide of Jun 2012

By: Lt Col Stefanie M. Watkins-Nance (RAM 2017) and Dr. Dan Van Syoc Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

## **CONDITION:**

**Anemia/Blood Loss/Bone Marrow Donation (Mar 2016)** 

## I. Waiver Consideration.

Anemia (hereditary, acquired, aplastic, or unspecified) does not meet retention standards and is disqualifying when symptomatic, or when response to therapy is unsatisfactory, or when therapy requires more than annual hematologist follow-up for all FC I/IA, FC II, FC III individuals, as well as all SWA and OSF personnel. For certification of ATC personnel, any anemia must be evaluated, but it may not be disqualifying if the member is asymptomatic and without identifiable causative etiology. Both symptomatic and asymptomatic anemia of any etiology, defined as hematocrit values less than 40% for men or 35% for women, is disqualifying for FC I/IA, FC II, FC III, and SWA duties. Anemia is not specifically disqualifying for GBO duties, but the underlying etiology may require aeromedical waiver. Minor, asymptomatic nutritionrelated anemia that fully responds to vitamin supplementation does not require a waiver. Evaluations are recommended for hematocrit values below 40% in men and 35% in women. The exact nature of the work-up should be guided by a thorough history and physical, but typically should include a complete blood cell count with red blood cell indices, peripheral smear, and reticulocyte count. Results from these may indicate the need for evaluation of iron or B<sub>12</sub> stores, hemoglobin electrophoresis, or possibly bone marrow biopsy. Donation of blood products (500mL or more) is disqualifying for 72 hours for aviators and 8 hours for RPA pilots and ATC personnel. RPA sensor operators and MOD personnel require only 4 hours of down time prior to return to duties

Table 1: Waiver potential for anemia\*

| Flying Class (FC)    | Waiver Potential  | ACS review/evaluation |
|----------------------|-------------------|-----------------------|
|                      | Waiver Authority† |                       |
| I/IA                 | Yes               | Maybe+                |
| Untrained II/III/ATC | AETC              |                       |
| II/III               | Yes               | Maybe+                |
|                      | MAJCOM            |                       |
| ATC/ SWA             | Yes               | No                    |
|                      | MAJCOM            |                       |
| GBO                  | N/A               | N/A                   |

<sup>\*</sup>Anemia excluding thalassemia and sickle cell.

<sup>†</sup>Symptomatic anemia, or anemia that has not been satisfactorily treated or requires continuing hematology follow-up requires an AFMRA waiver and MEB review for all.

<sup>+</sup>ACS review appropriate for any situation that needs further explanation or that the waiver authority wishes to have reviewed.

AIMWTS search in Jan 2016 revealed a total of 1309 cases of anemia with an aeromedical disposition; there were a total of 109 disqualifications in this group. Breakdown of the cases was as follows: 89 FC I/IA cases (13 disqualifications), 177 FC II cases (19 disqualifications), 700 FC III cases (58 disqualifications), 335 ATC/GBC cases (18 disqualifications) and 8 MOD cases (1 disqualification). Most of the FC III and ATC/GBC disqualifications were initial exams and the majority of the rest of the cases were disqualified for a diagnosis other than anemia.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. If an MEB is required due to continued symptomatic anemia, or anemia that has not been satisfactorily treated or requires continuing hematology follow-up, ensure the MEB result is included in the AMS.

Unless the waiver is for a chronic condition, most of these waivers would be expected to be indefinite.

The AMS for an anemia waiver (initial or renewal) should include the following:

- A. Complete history of the anemia event to include all treatments.
- B. Current labs to include complete blood cell count with red blood cell indices, peripheral smear, and reticulocyte count.
- C. Any consultation reports and special studies as applicable.

## III. Overview.

Anemia is a common problem with an estimated prevalence of 32.9% globally in 2010, notably higher in developing countries.<sup>1</sup> During 2010, there were 392,000 hospital discharges with anemia listed first as a diagnosis, with an average length of stay of 4.1 days.<sup>2</sup> In addition, the 237,000 visits to emergency departments with anemia as the primary hospital discharge diagnosis in 2011 is reflective of its commonality in the outpatient population as well.<sup>3</sup>

Simply described, anemia is a decrease in the individual's hemoglobin from their baseline.<sup>4</sup> Anemia is more specifically defined as a value more than 2 standard deviations below the mean. This equates to hemoglobin < 13.5 g/dL or a hematocrit < 41.0% in men, and <12.0 g/dL or < 36.0% for women.<sup>5</sup> The USAF Medical Standards Directory defines anemia as hematocrit values less than 40% for men and 35% for women.

Iron deficiency anemia is the most prevalent type of anemia. In fact, half of all cases worldwide are due to iron deficiency, particularly in the very young, those with poor nutrition, and women of childbearing age.<sup>6</sup> For American women ages 20-49, the prevalence is estimated to be as high as 11%.<sup>7</sup> Other less common etiologies for anemia include hemoglobinopathies, abnormal red cell membranes, and disturbed B<sub>12</sub> or folate absorption.<sup>8</sup>

Iron deficiency anemia can be caused by blood loss secondary to internal or external hemorrhage as well as blood donation. Occult bleeding can be difficult to evaluate in many people. Other

causes of iron deficiency include decreased iron absorption, certain foods and medications, celiac disease, and other more uncommon causes such as intravascular hemolysis and pulmonary hemosiderosis. Aside from hemorrhage, causes of anemia can be categorized as either hypoproliferative (impaired blood cell production) or hyperproliferative (hemolytic). 10

Blood donation is a common practice and is, in fact, promoted to the general and military populations through programs sponsored by the American Red Cross and Armed Services Blood Program. If an aircrew member is interested in platelet or plasma donation, it needs to be noted that this procedure (apheresis) can involve up to 800 mL in volume loss. As there is also some risk of hypocalcemia with this procedure, the member needs to be in a DNIF status for 72 hours after completion of the apheresis.

Iron deficiency anemia is theoretically simple to treat with medicinal iron supplementation. There are three available iron salts and these can be administered orally via tablet or elixir. Absorption of iron can be inhibited or enhanced by patient variables to include gastric acidity and use of other medications such as antacids. More recent studies on iron supplementation are stressing the importance of patient participation in their own care by helping their provider to identify a tolerable dose and dosing schedule.<sup>11</sup>

Bone marrow donation is also known as Stem Cell Harvest or Peripheral Blood Stem Cell Harvest. Civilians and military members may volunteer to donate bone marrow for either matched relatives or donor matches through the National Marrow Donor Program or C.W. Bill Young Department of Defense Marrow Donor Program (for more information, go to www.dodmarrow.org/ or www.dodmarrow.org/Pages/about/about\_program.htm).

# IV. Aeromedical Concerns.

Irrespective of the cause, anemia or blood volume loss can reduce tissue oxygenation and compromise organ function manifesting as fatigue, generalized weakness, decreased stamina, lightheadedness, chest pain, and decreased Gz tolerance. Physical exertion and hypoxia can further compromise function and overwhelm the body's capacity to compensate for the anemia. In younger patients, these symptoms may not be recognized until the hemoglobin is less than 7 or 8 g/dL.<sup>4</sup> More elderly patients may recognize these symptoms at hemoglobin levels of 9 to 11 g/dL while patients with chronic disease or gradual loss of red cell mass may report being asymptomatic at levels down to 5 to 6 g/dL. These clinical observations are based on patient data usually at low altitudes without extreme occupational exposures or duties.

For a patient with any baseline hemoglobin level, the above-noted symptoms will be more pronounced in the setting of acute blood loss, particularly if it is accompanied by loss of intravascular blood volume. A patient may tolerate up to 20% of acute blood volume loss with no cardiovascular compromise. In a recent study, it was found that the body replaces blood volume at an average of 36 days following a 550 cc whole blood donation. One study compared the changes in cardiovascular parameters and symptoms between donors who underwent sham, 1-unit, and 2-unit blood donations. There were no statistically significant differences between the groups. Nonetheless, it is still important to ensure that aviators do not exhibit any signs or symptoms of anemia. As a result, acute blood loss >500 mL (including blood donation) requires

grounding for at least 72 hours in manned aviation. As long as the flyer is feeling well, there is almost never a need to visit the FSO before resuming aviation duties.

Bone marrow (Stem Cell) donation is a more involved process than blood donation. Marrow may be donated via two methods. The first method involves actual harvest of stem cells from the donor bone marrow. In this method, patients are admitted to the hospital and may stay anywhere from 8 to 36 hours. Marrow is collected from the posterior-superior iliac spines or the sternum. The most common post-procedure symptoms include pain at the donor site (77%), fatigue (38%), nausea (25%), vomiting requiring intravenous medications (8%), and fever (5%). In order to accelerate recovery, some patients will choose to have autologous blood transfusions, but the overwhelming majority of patients never need a transfusion of any kind after donating bone marrow. Most women and some men also take oral iron replacement upon discharge. Pain resolves, on average, in 5.5 days with a range of 1 to 25 days. Full recovery of pre-procedure hemoglobin levels was observed at 3 months for males and 1 month for females. The authors noted that more females took iron supplementation than males in that study.

A second technique of bone marrow stem cell collection is peripheral blood stem cell (PBSC) apheresis.<sup>6</sup> PBSC apheresis is accomplished in an outpatient setting. With this collection method, the donor is given granulocyte colony-stimulating factors (GCSF) approximately one week before the collection. Once the donor's WBC count is sufficiently raised, stem cells are harvested from either an IV placed in the donor's arms or through a central catheter placed in the chest wall. The collection, similar in nature to a platelet donation, can usually be completed in 1-2 apheresis settings. The donor has minimal discomfort with this procedure and the side effects are limited to those of the GCSF administration. There is no prolonged anemia or recovery. The donor may have an elevated WBC for a few weeks following the donation.

Fliers who donate bone marrow should be DNIF until the following parameters have been met:

- surgical site has healed, and
- they deny any distracting pain, and
- stable follow-up hematocrit is above 32.

Oral iron supplements are compatible with flying status after successful ground testing. Iron injections may be administered to flying personnel while they are DNIF. No waiver is required following bone marrow donation.

| ICD-9 Codes | ICD-9 Codes for Anemia, Blood Loss, and Marrow Donations  |  |  |
|-------------|---|--|--|
| 280         | Iron Deficiency Anemia                                    |  |  |
| 281         | Other deficiency anemias                                  |  |  |
| 282         | Hereditary hemolytic anemias                              |  |  |
| 283         | Acquired hemolytic anemias                                |  |  |
| 284         | Aplastic anemia & other bone marrow failure syndromes     |  |  |
| 285         | Other and unspecified anemias                             |  |  |
| ICD-10 Code | ICD-10 Codes for Anemia, Blood Loss, and Marrow Donations |  |  |
| D50.9       | Iron Deficiency Anemia, unspecified                       |  |  |
| D50.8       | Other deficiency anemias                                  |  |  |
| D58.9       | Hereditary hemolytic anemia, unspecified                  |  |  |
| D59.9       | Acquired hemolytic anemia, unspecified                    |  |  |
| D61.89      | Other specified aplastic anemias & other bone marrow      |  |  |
|             | failure syndromes   |  |  |
| D64.9       | Anemia, unspecified                                       |  |  |

## V. References.

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- 2. National Summary Discharge Survey: 2010 Table, Average length of stay and days of care.
- 3. National Hospital Ambulatory Medical Care Survey: 2011 Emergency Department Summary Tables
- 4. Tefferi A. Anemia in Adults: A Contemporary Approach to Diagnosis. Mayo Clin Proc, 2003; 78: 1274-80.
- 5. Schrier SL. Approach to the adult patient with anemia. UpToDate. 24Jul 2015.
- 6. Bunn HF. Approach to the Anemias . Ch. 161 in Goldman: Goldman's Cecil Medicine, 24th ed., Elsevier, 2011.
- 7. Pottgiesser T, Specker W, Umhau M, et al. Recovery of hemoglobin mass after blood donation. Transfusion, 2008; 48: 1390-97.
- 8. Rayman RR, Davenport ED, Dominguez-Mompell R et al. *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., Castle Connolly Graduate Publishing LTD, New York, 2013; p. 160.
- 9. Schrier SL. Causes and diagnosis of iron deficiency anemia in the adult. UpToDate. Jul 23, 2015.
- 10. Marks PW. Approach to Anemia in the Adult and Child. Ch. 32 in *Hematology: Basic Principles and Practice*, 6<sup>th</sup> ed., Elsevier, 2013.
- 11. Alleyne M, Horne MK, and Miller JL. Individualized Treatment for Iron-deficiency Anemia in Adults. Am J Med, 2008; 121: 943-48.
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- 13. Gandini A, Roata C, Franchini M, et al. Unrelated allogenic bone marrow donation: short- and long-term follow-up of 103 consecutive volunteer donors. Bone Marrow Transplantation, 2001; 28: 369-74.

# **Ankylosing Spondylitis (Dec 2019)**

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS

Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

Significant Changes: Content updated to reflect national guidelines.

### I. Waiver Consideration

Ankylosing spondylitis and other nonradiographic axial spondylopathies are disqualifying for all flying classes, ATC duties, GBO duties, special warfare duties, and for retention if symptoms require duty restrictions, frequent absences from duty, ongoing specialty care follow-up greater than once per year, or disease-modifying antirheumatic drugs (DMARDs)/biologic therapies. Additionally, the chronic use of non-selective, non-steroidal anti-inflammatory drugs (NSAIDs) requires waiver for all classes except for GBO duties. Factors considered when assessing suitability for aeromedical waiver include the severity of disease at diagnosis, evidence of stable disease, whether treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the risk associated with specific medication(s), the individual service member's tolerance of the medication(s) and adherence to therapy, and the cumulative risk of all associated complications and/or extra-articular manifestations. Waiver can be considered once an individual is in disease remission on a stable, aeromedically-approved medication regimen, without adverse effects. Use of any medication not included on a career-field approved medication list is independently disqualifying and will be considered on a case-by-case basis.

Cervical spine involvement is relatively common in individuals with ankylosing spondylitis, predisposing individuals to atlantoaxial instability and/or atlantoaxial subluxation. Additionally, chronic inflammation of the axial skeletal system increases the risk of fracture and neurologic complications under forces generated during ejection. Thus, pilots eligible for waiver will be restricted to a FC IIB waiver, non-ejection seat aircraft. A restricted waiver might also be required for individuals assigned to rotary wing airframes due to the risk of disease progression under persistent vibration exposure in these airframes. Special warfare personnel may be restricted from jump status based on the severity of the underlying disease as well. These situations will be considered on a case-by-case basis.

**Table 1: Waiver potential for Ankylosing Spondylitis** 

| Flying Class (FC)         | Waiver Potential <sup>1</sup> | Waiver Authority        | ACS Review or Evaluation |
|---------------------------|-------------------------------|-------------------------|--------------------------|
| I/IA                      | No                            | AETC                    | No                       |
| II/III/Special<br>Warfare | Yes <sup>2,3,4</sup>          | MAJCOM <sup>2,3,4</sup> | Yes                      |
| ATC/GBO                   | Yes <sup>3,4</sup>            | MAJCOM <sup>3,4</sup>   | No                       |

- 1. Untrained personnel of any class are unlikely to receive an aeromedical waiver.
- 2. Waiver for pilots will be restricted to FC IIB. A FC IIC waiver, non-rotary wing aircraft, or restricted special warfare waiver precluding jump duties will be considered on a case-by-cases basis. AFMRA is the waiver authority for all restricted waivers and cases not meeting retention standards.
- 3. Use of any medication that is not included on the approved medication list is independently disqualifying, and the MAJCOM may disqualify the service member without AFMRA or ACS review. Waiver may be considered following an ACS review on a case-by-case basis in certain low-risk individuals treated with unapproved medications. The waiver authority for all non-approved medications is AFMRA.
- 4. Individuals controlled with TNF-alpha inhibitors require AF Form 469 document the need for access to transport and refrigeration (between 36 to 46 degrees Fahrenheit) for any TDY or deployment assignment.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

## A. <u>Initial Waiver Request:</u>

- 1 Summary of presentation, course, and treatment.
- 2 Consultation reports form treating rheumatologist, which should include:
  - a. Subjective symptoms and objective physical exam findings
  - b. Current treatment plan, to include tolerance and current doses of maintenance medications and all appropriate monitoring labs for those medications (e.g., biologic agents require CBC/CMP every 3-6 months and annual TB testing).
  - c. Documentation excluding/including extra-articular manifestations (i.e., ocular, pulmonary, cardiac, psoriasis, inflammatory bowel disease, etc.)
- 3 All pertinent laboratory studies, including diagnostic and follow-up results.
  - a. Initial serologic testing including HLA-B27
  - b. Recent CBC, CMP, ESR, and CRP.
- 4 Radiology reports from all diagnostic or follow-up imaging studies.
  - a. Initial and updated plain films of the lumbar spine and sacroiliac joints (Ferguson view)
  - b. Plain films of the cervical spine if indicated (i.e., neck or occipital pain)
- 5 Current physical examination findings with focus on musculoskeletal exam.

- 6 Echocardiogram if a murmur is auscultated.
- 7 Optometry or ophthalmology evaluation to exclude ocular involvement.
- 8 FL4 with RTD and ALC status, if applicable.
- 9 Any other pertinent information.
- 10 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Current symptoms and development of any disease flares, complications, or extraarticular manifestations.
  - b. Current medications, doses, and adverse effects.
  - c. Current physical examination findings.
- 2 Consultation reports from treating rheumatologist.
- 3 Any interval imaging obtained pertaining to the ankylosing spondylitis diagnosis.
- 4 Updated CBC, CMP, ESR, and CRP.
- 5 Updated plain films of the lumbar spine and sacroiliac (Ferguson view).
- 6 Updated dilated ocular exam.
- 7 Any other pertinent information.
- 8 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Ankylosing spondylitis (AS) is a chronic inflammatory disorder resulting in articular and extraarticular symptoms. The most common presentation is the development of inflammatory low back pain (morning stiffness > 30 minutes, pain improved with movement and worse with rest, nocturnal pain, etc.) that may result in significant occupational and functional limitation in the aviation environment. Untreated AS may result in damage and deformities including lumbar spinal fusion, sacral erosions, and cervical spine involvement to include atlantoaxial instability and atlantoaxial subluxation. The progressive nature and involvement of the axial spine in AS increases the risk of traumatic fractures and neurologic compromise. Thus, pilots submitting a waiver will be restricted to a FC IIB waiver, non-ejection seat aircraft. Persistent exposure to vibrations especially in rotary wing airframes increases the risk of disease progression. Thus, a FC IIC waiver, restricted to non-rotary wing airframes, may be warranted depending on the severity of the underlying disease. Additionally, special warfare personnel with significant disease may be restricted from jump status on a case-by-case basis. Ankylosing spondylitis is associated with the development of extra-articular involvement including anterior uveitis, apical pulmonary fibrosis, and cardiac abnormalities (i.e. aortic insufficiency, conduction abnormalities, etc.) that carry further aeromedical risk. Nonradiographic axial spondylopathies present similarly to AS except typical radiographic changes such as sacroiliitis are absent. Nonradiographic axial spondylopathies are associated with other systemic autoimmune disease such as psoriasis and inflammatory bowel disease.

Non-steroidal anti-inflammatory drugs (NSAIDs) are the initial treatment of choice along with physical therapy. Non-selective NSAIDs such as indomethacin have been shown to decrease

radiographic disease progression. Selective NSAIDs such as meloxicam and celecoxib are not as effective. Chronic use of non-selective NSAIDs requires a waiver for all flying classes except GBO personnel. There are multiple disease-modifying antirhuematic drugs and biologic agents used for the treatment of AS. The only career-field approved medications for treatment of AS are sulfasalazine, adalimumab, infliximab, and etanercept. Biologic agents such as adalimumab require access to transport and refrigeration (between 36 to 46 degrees Fahrenheit) for any TDY or deployment assignment.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 14 individuals with an AMS containing the diagnosis of AS. Two individuals (14.2%) were disqualified. A breakdown of the cases was follows: 0 FC I/IA cases, 11 FC II cases (1 disqualified), 2 FC III cases (1 disqualified), 0 ATC/GBC cases, 0 MOD cases, and 1 RPA Pilot cases (0 disqualified).

| ICD-9 codes for | ICD-9 codes for Ankylosing Spondylitis |  |
|-----------------|--|--|
| 720.0           | Ankylosing spondylitis                 |  |

| ICD-10 codes for Ankylosing Spondylitis |                                     |
|---|-------------------------------------|
| M45.9                                   | Ankylosing spondylitis, unspecified |

# IV. Suggested Readings

- 1. Lee JS, Lee S, Bang SY, et al. Prevalence and risk factors of anterior atlantoaxial subluxation in ankylosing spondylitis. *Journal of Rheumatology*. 2012; 39(12):2321-2326.
- 2. Smith SD, Jurcisn JG, Bowden DR. CV-22 Human Vibration Evaluation. AFRL-RH-WP-TR-2208-0095. April 2008.
- 3. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondyloarthritis research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Care & research. *Arthritis and Rheumatology*. 2019 Aug 22. doi: 10.1002/art.41042. https://www.ncbi.nlm.nih.gov/pubmed/31436036
- 4. Ward MM, Reveille JD, Learch TJ, et al. Occupational physical activities and long-term functional and radiographic outcomes in patients with ankylosing spondylitis. *Arthritis and Rheumatology*. 2008; 59(6):822-832.

### **WAIVER GUIDE**

Updated: May 2014

Supersedes Waiver Guide of Mar 2011

By: Col Bill Mueller, 711HPW/HP Pilot-Physician and Dr. Dan Van Syoc

### **CONDITION:**

Anthropometrics (Short Stature, Excessive Height, Weight, & Other Body Measurements) (May 2014)

## I. Waiver Considerations.

A waiver is required if the following values are exceeded on the initial flying class physical. There are no anthropometric standards for ATC, GBO, and SWA personnel. Initial RPA Pilot applicants are only required to meet GBO standards and obtain a FAA Class 3 medical certificate. In addition, there is a minimum functional reach of 76 inches for aeromedical evacuation crewmembers, regardless of their height. See Section T of the MSD for more detail.

Table 1: Waiver potential for anthropometric issues

| Condition      | FC I                 | FC IA, initial II, and | Waiver Potential      |
|----------------|----------------------|------------------------|-----------------------|
|                |                      | initial III            | Waiver Authority      |
| Height         | <64 inches or >77    | <64 inches or >77      | Possible‡             |
|                | inches               | inches*                | AETC/A2/3/10          |
| Sitting height | <34 inches or >40    | <33 inches or >40      | Possible‡             |
|                | inches               | inches (for initial FC | AETC/A2/3/10          |
|                |                      | IA and II)             |                       |
| Weight and     | If outside values of | If outside values of   | No waiver potential   |
| buttock-knee   | Table 1.             | Table 1.†              | for FC-I/IA because   |
|                |                      |                        | T-6 has ejection      |
|                |                      |                        | seat. Waiver for      |
|                |                      |                        | non-ejection seat a/c |
|                |                      |                        | for all others.       |
|                |                      |                        | AETC/A2/3/10          |

<sup>\*</sup> Weapons controllers/directors, combat control, pararescue and air battle managers do not require anthropometric waivers).

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

An AMS for anthropometric waivers should include the following:

• Required anthropometric measurements for the applicable flying class physical.

<sup>†</sup> Required for fighter track UNT, flight surgeons and any aircrew whose primary duties are in ejection seat aircraft.

<sup>‡</sup> FC I waiver eligibility depends on functional fit and safe-escape criteria. FC IA, II, and III waiver eligibility depends on safe-escape criteria only.

• If weight less than minimum standard, AMS should include weight history, review of systems, physical exam, and appropriate laboratory work up to rule out secondary causes.

### III. Overview.

In March 2003, the Chief of Staff of the Air Force (CSAF) announced a new process to manage CSAF Exception to Policy (ETP) requests for anthropometric waivers. As a result, individuals who do not meet AFI 48-123 Medical Standards Directory anthropometric standards can apply for a categorical waiver to enter flight training. Such categorical waivers would be limited to those aircraft in which the candidate meets 'functional fit' and 'safe-escape' standards. The criteria for 'functional fit' would be based on Air Force Research Lab (AFRL) cockpit anthropometric surveys of USAF aircraft. The criteria for 'safe-escape' would be based on ejection-seat design criteria. In his letter, CSAF designated AETC/CC, in coordination with AETC/SG, as the waiver authority for all anthropometric waivers. AETC/CC has delegated this waiver authority to the AETC/A2/3/10 (Director of Intelligence, Operations, and Nuclear Integration). Standing height, sitting height, buttock-to-knee length, and nude body weight are the screening measurements required for all initial Flying Class (FC) I, IA, II and III physicals to determine the need for further anthropometric clearance.

## STANDING HEIGHT and SITTING HEIGHT:

For initial FC I/IA, II and III, the standing-height limits are 64-77 inches. FC I applicants have a sitting height requirement of 34-40 inches and cannot exceed a buttock-to-knee of over 27.9 inches, while initial FC IA and II applicants have a sitting height requirement of 33-40 inches If outside this range, the applicant does not meet anthropometric standards and may be considered for an anthropometric waiver.

For FC I applicants seeking an anthropometric waiver, eight cardinal measurements must be performed at either the USAFA (for USAFA cadets) or the Medical Flight Screening (MFS) clinic at USAFSAM (for ROTC, OTS, and AD UFT Board Selectees). These measurements include: standing height, sitting height, buttock-knee-length, sitting knee height, arm span, sitting eye height, acromial height, and functional reach. These measurements are forwarded to AETC/SGPA for consideration of waiver potential. AETC/SGPA enters the cardinal measurements into a web-based Pilot Accommodation Study (PASS) computer program, which derives its data from the above mentioned AFRL study. The PASS program determines "functional fit" for all USAF aircraft as either "safe", "marginal", or "unsafe". Candidates with "safe" and "marginal" fits are able to adequately reach and manipulate the aircraft controls for that particular airplane.

After using the PASS program to assess functional fit, AETC/SGPA will make one of three possible waiver recommendations: unconditionally qualified, conditionally qualified for certain aircraft, or disqualified. This waiver recommendation is coordinated through AETC/A3F before final approval from AETC/A2/3/10.

The T-38 has the most restrictive anthropometric fit in the AF inventory. Since the T-38 is the pipeline aircraft to all fighters and bombers, conditional FC-I anthropometric waivers that exclude the T-38 also exclude fighters and bombers.

For non-pilot aircrew whose duties could be in an ejection seat aircraft (e.g. F-15E weapons system navigator, flight surgeon, aerial photographer, test-flight engineer), sitting height, butt-knee length and weight (discussed in WEIGHT section) must meet the minimum safe ejection seat requirements listed in Table 1. If outside these standards, then a conditional waiver will not include ejection-seat aircraft.

**Table 2: Ejection Seat Safe Escape Standards** 

| MAXIMUM VALUES (inches) (Minimum sitting height for all ejection seat aircraft is 33") |                  |                |               |  |
|--|------------------|----------------|---------------|--|
| Aircraft   | Butt-Knee Length | Sitting Height | Weight Limits |  |
| T-6  | 27.9             | 41.5           | 103-245       |  |
| T-38   | 30.8             | 40             | 103-240       |  |
| A-10   | 26.7*            | 43.6           | 103-245       |  |
| F-15   | 27.2             | 44.1           | 103-245       |  |
| F-16   | 27.1             | 39.7           | 103-245       |  |
| F-22   | 27.9             | 43.4           | 103-245       |  |
| B-1  | 28               | 44.4           | 103-245       |  |
| B-2  | 30.6             | 55.3           | 103-245       |  |
| B-52   | 28.4             | 53             | 103-245       |  |

<sup>\*</sup>Based on data obtained after an A-1- mishap.

# **WEIGHT**:

DODI 1308.3 (DoD Physical Fitness and Body Fat Programs Procedures) specifies weight standards which apply to all military members (may soon not apply to Air Force members). More restrictive weight criteria exist for safe-escape standards from ejection-seat aircraft. Specifically, nude body weight must be between 103 and 245 lbs (240 lbs for the T-38). Trained aircrew in ejection seat aircraft that fall outside these limits are placed on DNIF status until they meet standards. Trained aircrew flying ejection seat aircraft aircrew and not meeting weight standards may be considered for reassignment to a non-ejection seat aircraft. This process is managed by the operational chain of command and does not include a medical waiver for weight.

An individual who does not meet weight standards should be evaluated for primary medical causes of the weight gain/loss. If the evaluation rules out a pathologic cause, effective weight control may be obtained by an adequate dietary and physical exercise programs.

### IV. Aeromedical Concerns.

Height and weight extremes are concerns for functional fit and ejection. Functional fit takes into account the aircrew's angle of view over the nose of the aircraft and the ability to reach and actuate all controls. Improper functional fit due to anthropometric limitations can result in the inability to control the aircraft during certain phases of flight. During ejection, excessive height may be associated with increased neck and flail injuries because of positioning to accommodate the individual in the cockpit. Weight and stature also affects the center-of-gravity (CG) specifications of the ejection seat. The thrust mechanisms for ejection act behind the CG of the manned ejection seat. Therefore, low-weight can result in abnormal forward-pitch and interfere with man-seat separation and the parachute-opening sequence. Excessive weight alters the seat-aircraft separation sequence and the CG-parameters designed for the seat.

### V. References.

- 1. AETC Anthropometric Waiver Policy message, April 2003.
- 2. AETC/DO Anthropometric Waiver Policy Memorandum, 10 Mar 04.
- 3. AETC BBP on Anthropometric Waiver Policy, May 2005.
- 4. Air Force Instruction 36-2905 (Air Force Fitness Program). 1 Jul 2010.
- 5. Zehner GF, Hudson JA. Body Size Accommodation in USAF Aircraft. AFRL-HE-WP-TR-2002-0118.

# **Anxiety Disorders (Dec 2019)**

Reviewed: Lt Col Kevin F. Heacock (Chief, ACS Neuropsychiatry Branch), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Restructuring of Waiver Guide, Anti-depressant management, AIMWTS review

## I. Waiver Consideration

Anxiety disorders are disqualifying for all flying classes to include ATC, GBO and SWA duties, and may be disqualifying for continued service. Untreated or undertreated anxiety disorders may have potentially disastrous consequences. If the diagnostic criteria are met for specific phobia, social anxiety disorder, panic disorder, agoraphobia, generalized anxiety disorder, substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder, or unspecified anxiety disorder, the aviator is disqualified. Anxiety disorders tend to have a chronic clinical course with low rates of recovery and high likelihood of recurrence. One notable exception is for patients with specific phobia, who when treated early for a clearly defined fear have shown clinically significant improvement in 70-85% of cases treated with exposure therapy. For these reasons, a waiver is only likely in well-defined identifiable precipitating factors which are unlikely to reoccur.

To be considered for waiver, a mental health evaluation, with accurate diagnosis per the current Diagnostic and Statistical Manual (DSM), is the vital first step. USAF psychologists and/or psychiatrists familiar with aeromedical standards are the preferred choice for evaluation and potential development of the treatment plan. If the diagnosis of an anxiety disorder is established, then grounding the aviator is necessary to allow optimal treatment to be initiated. Psychotherapy, healthy lifestyle interventions, and/or psychotropic medications may be utilized as treatment options until anxiety symptoms are fully resolved (an important goal because partial resolution of symptoms may lead to long-term psychiatric morbidity). Psychotherapy may be continued after symptom resolution to bolster resiliency and coping mechanisms.

Antidepressants are usually the psychotropic agent of choice if healthy lifestyle interventions and psychotherapy have not achieved full resolution of symptoms. Clinical judgment is required for the duration of the antidepressant treatment (maintenance treatment phase), often dictated by the duration of anxious symptoms which prompted the treatment. In treating a first episode of major depressive disorder, antidepressants are typically continued for 6-12 months after full resolution of depressive symptoms in order to prevent abrupt relapse after medication cessation. Since there are no comparable guidelines for length of recommended maintenance treatment of anxiety, clinical judgment is necessary.

In 2013, the USAF began allowing select FC II/III personnel to be considered for waivers on antidepressants. After 5 years of observation, in 2018 the USAF allowed all aviators, including single seat and B-2 pilots, to be considered for waivers on the following monotherapies:

- 1. Sertraline (Zoloft®) up to 200 mg/day
- 2. Citalopram (Celexa®) up to 40 mg/day
- 3. Escitalopram (Lexapro®) up to 20 mg/day
- 4. Bupropion (Wellbutrin®) SR or XL up to 400 mg/day or 450 mg/day, respectively

Of these approved medications, Wellbutrin is known to be less effective in treating anxiety disorders. Also, the dosage of the antidepressant tends to require "higher than usual" amounts when treating anxiety as compared to treatment for depression. This often makes Zoloft an attractive choice in treating anxiety among these approved antidepressants.

The aviator on a maintenance antidepressant (only one aeromedically approved medication allowed) needs to be on the medication and remain clinically asymptomatic for at least 6 months before waiver consideration. The dose of the medication can be adjusted to maximize treatment and/or limit side effects without restarting this 6 month period as long as the aviator's symptoms remain stable. If a psychotropic medication is ever adjusted in dose or discontinued in an aviator, two weeks of observation should occur before considering resuming full flight duties to assure no adverse/unexpected side effects or return of symptoms occur. If symptoms return after discontinuing treatment, a return to, or enhancement of, psychotherapy, healthy lifestyle interventions, and/or antidepressant medication for maintenance treatment should be considered.

**Table 1: Waiver potential for anxiety disorders** 

| Flying Class (FC) | Waiver Potential     | ACS Review/Evaluation |
|-------------------|----------------------|-----------------------|
|                   | Waiver Authority     |                       |
| I/IA              | Maybe <sup>1</sup>   | At the request of the |
|                   | AETC                 | waiver authority      |
| II/III            | Maybe <sup>1,2</sup> | At the request of the |
| ATC/GBO/SWA       | MAJCOM               | waiver authority      |

<sup>1.</sup> For all UNTRAINED individuals in any flying class (FC I/IA, FC II/III, or ATC/GBO/SWA), a waiver is NOT considered if they are currently taking an antidepressant. A waiver for an untrained individual with a history of an anxiety disorder is unlikely, unless there are well-defined identifiable precipitating factors which are unlikely to reoccur. A waiver is considered after the anxiety is completely resolved and medications and/or psychotherapy have been discontinued for a minimum of 2 years.

## **II. Information Required for Waiver Submission**

## A. <u>Initial Waiver Request:</u>

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder.
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

## B. Renewal Waiver Request:

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder.
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

<sup>2.</sup> For trained personnel, a waiver is considered after anxiety is completely resolved and stability, on or off medication, has been demonstrated for 6 months. A waiver is only likely in well-defined identifiable precipitating factors which are unlikely to reoccur.

# Please feel free to contact the ACS Neuropsychiatry Branch with questions:

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### III. Aeromedical Concerns

Many of the emotional and behavioral manifestations of anxiety disorders can interfere with flying safety and mission completion. Severe anxiety can markedly impair the ability to focus and concentrate on the task at hand. Trembling may diminish the ability to manipulate controls. Palpitations, shortness of breath, chest pain, nausea, and dizziness may be significantly distracting. Some of the more severe symptoms of anxiety, such as those seen in panic disorder (overwhelming anxiety, derealization, and fear of losing control) may be acutely incapacitating. Anxiety is often a factor in depression and psychosomatic complaints as well as being associated with substance misuse, particularly alcohol. Clinical levels of situational or chronic anxiety raise concerns regarding an aviator's emotional stamina and resilience needed to manage the inherent dangers and rigors associated with flying, especially during austere and deployed conditions. It should also be noted that anxiety stemming from a chronically high operational tempo, large workload, and accumulating life stressors may manifest itself as low motivation to fly. The aeromedical disposition of flight personnel diagnosed with an anxiety disorder depends on the specific category of the disorder and phase of the illness.

Anxiety disorders are generally characterized by fear/apprehension, obsessions, fear of loss of control, and physiological symptoms severe enough to interfere with social or occupational functioning. Anxiety is seen in many other psychiatric disorders, but in its benign form, is part of normal emotional experience. Symptomatic anxiety can be constant or nearly so, as in generalized anxiety disorder, or episodic. Episodic spells of anxiety can begin without warning or provocation, as in panic disorder, or predictably in certain situations, as in simple or social phobia. In the latter case, efforts to avoid the anxiety-provoking stimulus can drastically impact the aviator's lifestyle.

## **Special Considerations**

Three terms that relate specifically to anxiety and flying are often used in aerospace medicine. These are: manifestations of apprehension (MOA), fear of flying (FOF), and phobic fear of flying (specific phobia in DSM-5). MOA and FOF are used to denote a non-phobic fear based on uneasiness, lack of motivation, feelings of inadequacy, rational decision, life circumstance, etc.; MOA is used with student aviators and FOF for rated/trained aviators. Both MOA and FOF are handled administratively by the commander (often in the context of a flying evaluation board or the SUPT/UNT equivalent). A mental health consultation is helpful to clarify the issues in MOA and FOF, and to help rule out a true anxiety disorder. An increasingly recognized problem in the ATC/GBC community is fear of controlling. Similar to fear of flying, these cases are almost always handled administratively.

Phobic fear of flying is a true phobia, often involving only flying, though the symptoms can broaden to other areas of life if not treated. Phobic fear of flying is handled like the other anxiety disorders: by medical disqualification, referral to mental health for evaluation and treatment, and then a return to flying when the disorder is resolved. Persistence of anxiety symptoms, despite adequate treatment or a reluctance to enter treatment, should raise questions about the aviator's motivation to fly.

AIMWTS review in Nov 2019 revealed 341 cases since 1 Jan 2015 with a diagnosis of an anxiety-related disorder. Of these, 168 (49%) were disqualified. Breakdown of the cases revealed: 29 FC I/IA cases (17 disqualified), 51 FC II cases (14 disqualified), 20 RPA pilot cases (12 disqualified), 164 FC III cases (84 disqualified), 66 ATC/GBC cases (37 disqualified), 7 Special Warfare Airmen cases (3 disqualified), and 4 MOD cases (1 disqualified).

| ICD 9 codes fo | r anxiety disorders                      |  |
|----------------|--|--|
| 291.89         | Alcohol-Induced Anxiety Disorder         |  |
| 292.89         | Substance/Medication-Induced Anxiety     |  |
|                | Disorder (name specific substance)       |  |
| 293.84         | Anxiety Disorder Due to Another General  |  |
|                | Medical Condition                        |  |
| 300.00         | Unspecified Anxiety Disorder             |  |
| 300.01         | Panic Disorder                           |  |
| 300.02         | Generalized Anxiety Disorder             |  |
| 300.09         | Other specified Anxiety Disorder         |  |
| 300.22         | Agoraphobia                              |  |
| 300.23         | Social Anxiety Disorder (Social Phobia)  |  |
| 300.29         | Specific Phobia (formerly Simple Phobia) |  |
| 300.3          | Obsessive-Compulsive Disorder            |  |

| ICD-10 codes for anxiety disorders |  |  |  |
|------------------------------------|--|--|--|
| F41.9                              | Anxiety Disorder, Unspecified                |  |  |
| F41.0                              | Panic Disorder (episodic paroxysmal anxiety) |  |  |
|                                    | without Agoraphobia                          |  |  |
| F41.1                              | Generalized Anxiety Disorder                 |  |  |
| F40.01                             | Agoraphobia with Panic Disorder              |  |  |
| F40.02                             | Agoraphobia without Panic Disorder           |  |  |
| F40.10                             | Social Phobia, Generalized                   |  |  |
| F40.11                             |  |  |  |
| F42                                | Obsessive-compulsive disorder                |  |  |
| F06.4                              | Anxiety Disorder Due to Known                |  |  |
|                                    | Psychological Condition                      |  |  |
| F19.980                            | Other Psychoactive Substance Use,            |  |  |
|                                    | Unspecified with Psychoactive Substance-     |  |  |
|                                    | Induced Anxiety Disorder                     |  |  |

# **IV. Suggested Readings**

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### **WAIVER GUIDE**

Initial Version: Dec 2015

Supersedes Waiver Guides of Aug 2014 (Bicuspid Aortic Valve), Oct 2010 (Aortic Insufficiency),

and Oct 2010 (Aortic Stenosis)

By: Dr Dan Van Syoc, Dr. Eddie Davenport (ACS Chief Cardiologist)

### **CONDITION:**

**Aortic Valve Disease (Dec 2015)** 

## I. Waiver Consideration.

All flying classes except are disqualified for aortic valve insufficiency (AI) greater than trace, any degree of aortic stenosis (AS), and bicuspid aortic valve (BAV) (regardless of degree of AI & AS).

ACS review is required for waiver consideration. ACS evaluation may be required, depending on the flying class or for specific concerns in an individual case. Waiver recommendations are primarily dependent on the presence and severity of associated AS and AI. FC I and IA will only be waiver eligible for BAV with ≤ mild AI and no AS; any greater AI or any AS is not waiver eligible. FC II/III requires ACS evaluation for waiver consideration. ACS re-evaluations will be performed at 1-3 year intervals, depending on the degree of AI and/or AS and other related conditions such as chamber dilation, left ventricular function and left ventricular hypertrophy. As discussed above, the use of approved ACE inhibitors and nifedipine for afterload reduction is acceptable in aviators with BAV and asymptomatic moderate or severe AI.³ Waiver may be considered after surgery; please refer to the "Valve Surgery − Replacement or Repair" waiver guide. Table 2 is a summary of the clinical manifestations and most common requirements for the separate flying class (FC) duties for BAV, table 3 summarizes recommendations for AI in a structurally normal valve, and table 4 summarizes recommendations for AS in a structurally normal valve.

Table 1. Summary of BAV and Associated Clinical Conditions and ACS Requirements.

| BAV and Associated Levels of          | Flying Class      | Waiver    | Required ACS   |
|---------------------------------------|-------------------|-----------|----------------|
| Aortic Stenosis (AS) and/or           | Trying Class      | Potential | Review and/or  |
| Aortic Insufficiency (AI)             |                   | Waiver    | ACS Evaluation |
| Aortic insufficiency (A1)             |                   | Authority | ACS Evaluation |
| BAV with no, trace or mild AI         | FC I/IA           | Yes       | ACS review     |
| (≤mild) and no AS                     | I'C I/IA          | AETC      | ACS leview     |
|                                       |                   | ALIC      |                |
| BAV with >mild AI or any AS           | FC I/IA           | No        | ACS review     |
| Bit with a mind in or this is         |                   | AETC      | TICSTOVICW     |
|                                       |                   | TILI C    |                |
|                                       | FC II, GBO        | Yes       | ACS review     |
|                                       | ATC, SWA          | MAJCOM    |                |
|                                       |                   |           |                |
| BAV with $\leq$ mild AI and/or $\leq$ | FC II/III**       | Yes       | ACS evaluation |
| mild AS                               |                   | MAJCOM    |                |
|                                       |                   |           |                |
|                                       | ATC/GBO/SWA       | Yes       | ACS review     |
|                                       |                   | MAJCOM    |                |
| BAV with moderate AI and/or           | FC IIA (non-SHGA  | Yes       | ACS evaluation |
| greater than mild AS†                 | only)             | AFMRA     |                |
|                                       |                   |           |                |
|                                       |                   | Yes       | ACS evaluation |
|                                       | FC III,           | AFMRA     |                |
|                                       | ATC/GBO/SWA       |           |                |
|                                       | (low performance  |           |                |
|                                       | only)             |           |                |
| BAV with severe AI only –             | FC IIA only       | Maybe*    | ACS evaluation |
| asymptomatic and nonsurgical          |                   | AFMRA     |                |
| AI per guidelines                     |                   |           |                |
|                                       | FC III (low       | Maybe*    | ACS evaluation |
|                                       | performance only) | MAJCOM    |                |
|                                       | A TIC/CD O/CIVA   | 3.5       | A COR D        |
|                                       | ATC/GBO/SWA       | Maybe     | ACS Review     |
|                                       |                   | MAJCOM    | 1.00           |
| BAV with $\geq$ moderate AS† or       | FC II/III         | No        | ACS review     |
| with severe AI‡ surgical by           |                   | AFMRA     |                |
| guidelines                            | ATIC/CIVIA/CIPO   | 3.6       | A CCC          |
|                                       | ATC/SWA/GBO       | Maybe     | ACS review to  |
|                                       |                   | AFMRA     | confirm        |

<sup>\*</sup> Waiver in untrained FC II and III individuals unlikely.
† Moderate to severe AS requires medical evaluation board (IRILO/MEB).

<sup>‡</sup> Severe AI if symptomatic and associated with left ventricular dilation or dysfunction requires IRILO/MEB.

Table 2: Summary of waiver potential and required ACS evaluation for degrees of AI in aircrew.

| Degree of Aortic<br>Insufficiency (AI)               | Condition                         | Flying Class                  | Waiver Potential/ Waiver Authority  | Required ACS<br>Review and/or<br>ACS Evaluation |
|--|-----------------------------------|-------------------------------|-------------------------------------|---|
| Trace  | Trileaflet<br>aortic valve        | Qualifying for all classes    | Not required<br>(Normal<br>variant) | ACS review to confirm                           |
|  | Bicuspid<br>aortic valve<br>(BAV) | FC I/IA                       | Yes<br>AETC                         | ACS evaluation                                  |
|  |                                   | FC II                         | Yes<br>MAJCOM                       | ACS evaluation                                  |
| Mild   | Trileaflet or BAV***              | FC I/IA                       | Yes<br>AETC                         | ACS evaluation.                                 |
|  |                                   | FC II/III<br>ATC/SWA/GBO      | Yes<br>MAJCOM                       | ACS evaluation                                  |
| Moderate   | Trileaflet or<br>BAV              | FC I/IA                       | No<br>AETC                          | ACS review to confirm                           |
|  |                                   | FC IIA                        | Yes*<br>AFMRA                       | ACS evaluation                                  |
|  |                                   | FC III (low performance only) | Yes*<br>MAJCOM                      | ACS evaluation                                  |
|  |                                   | ATC/GBO/SWA                   | Yes<br>MAJCOM                       | ACS review                                      |
| Severe – asymptomatic and nonsurgical per guidelines | Trileaflet or<br>BAV              | FC IIA only                   | Maybe*<br>AFMRA                     | ACS evaluation                                  |
|  |                                   | FC III (low performance only) | Maybe*<br>MAJCOM                    | ACS evaluation                                  |
|  |                                   | ATC/GBO/SWA                   | Yes<br>MAJCOM                       | ACS review                                      |
| Severe – symptomatic or surgical per guidelines†     | Trileaflet or<br>BAV              | FC II/III                     | No<br>MAJCOM                        | ACS review                                      |
|  |                                   | ATC/GBO/SWA                   | Maybe<br>MAJCOM                     | ACS review                                      |

<sup>\*</sup> Waiver in untrained FC II and III unlikely.
† Medical evaluation board (MEB) required.
\*\* GBO, SWA, and ATC waivers for mild disease are very likely to be approved.

Table 3: Summary of Degree of Aortic Stenosis and ACS Requirements.

| <b>Associated Levels of</b>                     | Flying Class      | Waiver          | Required ACS Review   |
|---|-------------------|-----------------|-----------------------|
| Aortic Stenosis (AS)                            |                   | Potential       | and/or ACS Evaluation |
|   |                   | Waiver          |                       |
|   |                   | Authority       |                       |
| Mild AS   | FC I/IA           | No<br>AETC      | ACS review to confirm |
|   | FC II/III         | Yes<br>MAJCOM** | ACS evaluation        |
|   | ATC/GBO/SWA       | Yes<br>MAJCOM   | ACS review to confirm |
| Mild-to-moderate AS                             | FC IIA            | Yes             | ACS evaluation        |
| (greater than mild not meeting all criteria for | (low G- aircraft) | AFMRA           |                       |
| moderate based on ACS                           | FC III            |                 |                       |
| review)   | (low G- aircraft) | Yes<br>MAJCOM   | ACS evaluation        |
|   | ATC/GBO/SWA       | Yes<br>AETC     | ACS review to confirm |
| ≥ Moderate AS*                                  | FCI/IA, II, III   | No              | ACS review to confirm |
|   | ATC/GBO/SWA       | Maybe<br>AFMRA  | ACS review to confirm |

<sup>\*</sup> Medical evaluation board (MEB) required.

AIMWTS search in Dec 2015 for aortic valve disease revealed 372 cases. Breakdown of the cases revealed: 41 FC I/IA cases (8 disqualified), 227 FC II cases (23 disqualified), 89 FC III cases (20 disqualified), 6 ATC/GBC cases (1 disqualified), and 9 MOD cases (1 disqualified). There was significant overlap in these cases and the vast majority were mild and well controlled.

## II. Information Required for Waiver Submission.

Aeromedical Consultation Service (ACS) review/evaluation is required for all classes of flying duties for BAV with or without AI/AS, as well as for AI or AS without BAV. No additional studies are routinely required prior to ACS evaluation. If however, the treating physician deems it clinically necessary to perform additional studies, it is required that all studies be forwarded to the ACS for review. There is no minimum required non-flying observation period for waiver consideration for BAV, regardless of the presence or severity of AI or AS.

The aeromedical summary for <u>initial waiver</u> for aortic valve disease (initial ACS evaluation) should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. Complete history and physical examination to include detailed description of symptoms, medications, activity level, family history, and CAD risk factors (positive and negative).
- C. Copy of the local echo report and videotape or CD copy of the echo documenting BAV. (Notes 1 and 2)
- D. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. Holter, treadmill, stress echocardiogram). (Notes 1 and 2)
- E. Additional local cardiac testing is not routinely required but may be requested in individual cases.
- F. Results of IRILO/MEB, if required.

The aeromedical summary of <u>waiver renewal</u> for aortic valve disease (ACS follow-up evaluations) should include the following:

- A. Complete history and physical examination to include detailed description of symptoms, medications and activity level.
- B. Local follow-up cardiac testing is not routinely required prior to ACS re-evaluation. However, in asymptomatic individuals with mild or less AS/AI, it is common for the ACS to make a recommendation based on local AMS, ECG, and echocardiogram. This often will be specified in the report of the previous ACS evaluation.
- C. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. Holter, treadmill, stress echocardiogram). (Notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

To expedite the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

## III. Overview.

Aortic valvular disease is relatively common in our aviation population. Previous waiver guides have separately addressed bicuspid aortic valve, aortic insufficiency, and aortic stenosis. As there is significant overlap of these conditions, this new waiver guide will discuss all three together.

## Bicuspid Aortic Valve (BAV)

BAV occurs in 1-2% of the general U.S. population and is the most common congenital cardiac malformation, excluding mitral valve prolapse. BAV and calcified aortic valve are the most common causes of chronic aortic regurgitation in the US and developed countries. The

prevalence of BAV is 0.6% in the United States Air Force (USAF) based on a database of over 20,000 Medical Flight Screening echocardiograms (echo) performed on pilot training candidates.<sup>3,4</sup> Based on current ACS database review 84% of BAV subjects will develop some degree of aortic stenosis (AS) and/or aortic insufficiency (AI) during their lifetime. Additionally, 30-40% will require aortic valve replacement during their lifetime, predominantly after age 45.<sup>3,4</sup> There is an association of BAV with aortopathy and thus CT angiography of the aorta is recommended if the morphology of aortic sinuses, sinotubular junction, or ascending portion cannot be assessed accurately or fully by echocardiography or when the aortic diameter appears greater than 4.0 cm on echocardiography.<sup>2</sup> There is some more recent published data that may support one evaluation of the ascending aorta via CT Aorta with contrast even without any signs or symptoms or aortopathy. Waiver criteria is largely based on degree of AI or AS as below, however even in the absence of AS or AI, waiver is still required given the high progression rates of BAV. Waiver for BAV with no or trace AI will typically be followed every three years with echocardiography

# Aortic Insufficiency/Regurgitation

Aortic Insufficiency (AI), particularly in its milder forms, is usually asymptomatic for decades due to the compensation of the left ventricle to the volume overload produced by this condition. Symptoms generally do not become clinically apparent until some degree of left ventricular (LV) failure has occurred, usually after the fourth decade of life. AI is therefore most commonly associated with symptoms related to left ventricular failure, (e.g., exertional dyspnea, orthopnea, fatigue, and paroxysmal nocturnal dyspnea). Symptoms of angina are rare in the absence of coronary artery disease. The severity of AI is graded as trace, mild, moderate or severe. Trace AI is considered to be a physiologically normal variant in the absence of an accompanying AI murmur and with a structurally normal three-leaflet valve. The natural progression of AI varies based on symptoms and LV dysfunction as listed below. There is very little published data on the natural history of the progression of AI, particularly the mild to moderate types in a structurally normal valve. However, in an ACS review of 877 cases of Aortic Valve insufficiency followed over 10 years, progression rates from mild insufficiency to moderate was 8%, and progression rates from moderate to severe insufficiency was 23%. In a review of all cases of any valvular regurgitation, the aortic valve was most likely to have moderate or greater insufficiency on screening echocardiography, and the only valve in which mild insufficiency progression rates were >2%. Severe AI has a worse prognosis as seen below.

Table 4: Natural History of Severe Aortic Insufficiency<sup>5</sup>

| Asymptomatic patients with normal LV systolic function             |            |
|--|------------|
| <ul> <li>Progression to symptoms and /or LV dysfunction</li> </ul> | <6%/year   |
| <ul> <li>Progression to asymptomatic LV dysfunction</li> </ul>     | <3.5%/year |
| Sudden death   | <0.2%/year |
| Asymptomatic patients with LV systolic dysfunction                 |            |
| Progression to cardiac symptoms                                    | >25%/year  |
| Symptomatic patients   |            |
| Mortality rate   | >10%/year  |

Although there is a low likelihood of patients developing asymptomatic LV dysfunction, more than one fourth of the patients who die or develop systolic dysfunction will do so prior to the onset of any warning symptoms.

In a clinical population, AI is caused by aortic root or leaflet pathology. Root pathology is most commonly caused by dilatation associated with hypertension and aging. Other root pathologies include Marfan's syndrome, aortic dissection, ankylosing spondylitis and syphilis. Leaflet pathologies include infective endocarditis, bicuspid aortic valve and rheumatic heart disease. In the aviator population, the most common etiologies will be idiopathic AI with normal aortic valve and root and bicuspid aortic valve.

Theoretical concerns exist that extreme athletic activity or isometric exercise, or activities which include a significant component of such exercise, may promote progression of this condition and should therefore be discouraged. Examples of such activities would include the anti-G straining maneuver, weight lifting, and sprint running. Published guidelines for athletes with AI restrict activities for those with the moderate and severe types. Therefore, moderate AI and asymptomatic severe AI that does not meet guidelines criteria for surgery are restricted to nonhigh performance aircraft. Symptomatic severe AI and severe AI meeting guidelines criteria for surgery are disqualifying and waiver is not recommended. Moderate to severe AI should be followed closely, preferably by a cardiologist, for development of criteria for surgical intervention and to address the need for vasodilator therapy. Medications to reduce afterload, such as ACE inhibitors and nifedipine, have documented clinical benefit in chronic AI of moderate or greater severity especially if blood pressure is elevated. These medications can delay the need for surgery and improvement of surgical outcome. The use of approved ACE inhibitors and nifedipine is therefore acceptable in aviators with asymptomatic moderate and severe AI (although waiver still required).<sup>3</sup> An echocardiogram with Doppler flow study easily diagnoses AI and is the mainstay of severity assessment. In addition, left ventricular function and chamber size impact the assessment of the severity of disease.

### **Aortic Stenosis**

Aortic stenosis (AS) usually occurs at the level of the aortic valve. Supravalvular and subvalvular forms of AS exist but are unusual congenital defects less likely to present as a new diagnosis in adult military aviator/aircrew. These would be addressed aeromedically on a case-by-case basis. Valvular AS has several causes. In older adults the most common is senile AS, an aging-related calcifying, degenerative process. In the military aviator/aircrew population the most common cause will be associated bicuspid aortic valve. AS is still unusual in military aviator/aircrew with bicuspid aortic valve because this complication usually occurs in middle-aged or older patients.<sup>3, 4</sup>

While the diagnosis may be suspected by careful auscultation, AS is primarily an echocardiographic (echo) diagnosis. On echo AS is graded by a combination of mean pressure gradient across the stenotic valve and calculated valve area. Grading categories are mild, moderate and severe.<sup>1, 3, 4, 5</sup> The prognosis of mild AS is good and essentially normal for at least five years after diagnosis however progression is common and thus disqualifying for all pilot candidates (FCI/IA). Once AS has progressed to moderate or severe, aeromedical and clinical concerns also include sudden cardiac death, syncope, angina and dyspnea. Angina may occur in

the absence of significant coronary atherosclerosis while dyspnea may appear as a result of left ventricular dysfunction. Event rates are 5% and 10% per year for asymptomatic and symptomatic moderate AS, respectively. Event rates are considerably higher for severe AS. Mild-to-moderate AS has normal expected event rates for 1-3 years, but represents AS that is likely progressing toward moderate and later severe AS. At this level of stenosis, maintenance of normal cardiac output under +Gz load is a potential aeromedical concern, prompting restriction from high performance flying duties.

## Antibiotic Endocarditis Prophylaxis for Aortic Valve disease

In early 2007, the American Heart Association published new infective endocarditis guidelines that are dramatically different from past recommendations. Subsequently endocarditis prophylaxis was recommended only for specified high risk groups, and only for dental procedures, respiratory tract procedures, and procedures on infected skin, skin structures or musculoskeletal tissue. The high risk group was limited to prosthetic cardiac valves, previous endocarditis, select congenital heart conditions and cardiac transplant patients with valvulopathy. Prophylaxis was no longer recommended for gastrointestinal or genitourinary procedures. Conditions commonly seen by most aerospace medicine practitioners were not included in the list of high risk conditions. Such common conditions no longer recommended for endocarditis prophylaxis include bicuspid aortic valve and aortic regurgitation with normal valve morphology.

## IV. Aeromedical Concerns.

Aeromedical concerns include the development and progression of AS and/or AI. Risk of a sudden incapacitating event is very low and aeromedically acceptable in the absence of significant AS or AI. Aeromedical concerns include: related symptoms such as exertional dyspnea, orthopnea and paroxysmal nocturnal dyspnea. Also the progression of AI or AS to greater than mild and the impact of the anti-G straining maneuver or isometric/dynamic exercise on the degree of AI/AS which could result in reduced cardiac output and hypoperfusion of the brain are additional concerns. Any requirement for medical therapy, such as vasodilators are important concerns for aircrew with AI/AS. Waiver policies are thus primarily dependent on the presence and severity of associated AS and AI. AI and AS severity is graded by echo as: mild, moderate and severe (AI can also be trace).<sup>3</sup> Asymptomatic BAV in USAF aviators was recently reviewed with 10 year progression rates of 10% for AS, 84% for AI, and 0.8% for endocarditis.<sup>7</sup> Progression to severe AI or AS or symptoms requiring valvular replacement was 2%. Progression rates of moderate valvular regurgitation to severe is greater than 20% over 10 years.<sup>8</sup> Aeromedical risks of aortopathy which can be associated with BAV include dissection and rupture and thus a one-time CT angiography of the aorta is recommended for aviators with BAV if not well visualized or dilated on echocardiography. Aeromedical concerns for AS include progression to significant stenosis and requirement for aortic valve replacement or repair. The prognosis of mild AS is good and essentially normal for at least five years after diagnosis. Once AS has progressed to moderate or severe, aeromedical and clinical concerns also include sudden cardiac death, syncope, angina and dyspnea. Angina may occur in the absence of significant coronary atherosclerosis while dyspnea may appear as a result of left ventricular dysfunction. Event rates are 5% and 10% per year for asymptomatic and symptomatic moderate AS, respectively. Event rates are considerably higher for severe AS. Mild-to-moderate AS has

normal expected event rates for 1-3 years but represents AS that is likely progressing toward moderate and later severe AS. At this level of stenosis, maintenance of normal cardiac output under +Gz load is a potential aeromedical concern, prompting restriction from high performance flying duties.<sup>3</sup>

| ICD 9 codes for Aortic Valve Disease |   |  |
|--------------------------------------|---|--|
| 395.0                                | Rheumatic aortic stenosis                           |  |
| 395.1                                | Rheumatic aortic regurgitation                      |  |
| 395.2                                | Rheumatic aortic stenosis with aortic regurgitation |  |
| 395.9                                | Other and unspecified rheumatic aortic disease      |  |
| 396.0                                | Mitral valve stenosis and aortic valve stenosis     |  |
| 424.1                                | Aortic valve disorders                              |  |
| 746.4                                | Congenital insufficiency of aortic valve            |  |

| ICD 10 codes for Aortic Valve Disease |   |  |
|---------------------------------------|---|--|
| I06.0                                 | Rheumatic aortic stenosis                           |  |
| I06.1                                 | Rheumatic aortic regurgitation                      |  |
| I06.2                                 | Rheumatic aortic stenosis with aortic regurgitation |  |
| I06.8                                 | Other rheumatic aortic diseases                     |  |
| Q23.1                                 | Congenital insufficiency of aortic valve            |  |
| I35.8                                 | Other non-rheumatic aortic valve disorders          |  |

### V. References.

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### **WAIVER GUIDE**

Updated: March 2020

Supersedes Waiver Guide of Sept 2015

By: Lt Col Dara D. Regn, ACS Pulmonologist

# **CONDITION:**

Asthma (Mar 2020)

## I. Waiver Consideration.

Any type of asthma or history of asthma is disqualifying for all flying duties as well as for ATC/GBO and SWA personnel, as well as retention. Although some data suggests that the age of waiverable childhood asthma could potentially be lowered, current policy makers have left the regulation as it has been for the past several years. A history of childhood asthma prior to the 13<sup>th</sup> birthday is waiverable; after age 12 (after the 13<sup>th</sup> birthday) waiver is not generally granted on initial flying physicals.

For trained aircrew, asthma and exercise induced bronchospasm (EIB) may be waivered for FC II and FC III, after ACS review. Use of more than three metered-dose SABA inhalers per year is suspicious for utilization as rescue treatment. If evidence of established asthma is present, waiver is still possible, but the patient should be well treated, usually with an aircrew-approved controller medication.

Since ICS and montelukast both show efficacy for exercise-induced symptoms in established asthma, use of SABA should not be necessary. The sole exception would be a flare associated with a respiratory infection, during which the aviator should be DNIF. If such a flare occurs, the individual should remain DNIF for one week after stopping use of SABA, to allow the inflammatory process to resolve. The ACS typically performs a methacholine challenge test (MCT) on all members requesting a waiver for asthma and an exercise challenge in those with history of exercise induced symptoms. This test is done on patients, while they are taking their controller medications to measure their level of residual bronchial hyper-reactivity. In the ACS's experience, asthmatics who require rescue inhaler use, even rarely, typically fail their methacholine challenge tests and are not granted waivers. For this reason, it is of paramount importance for the local flight surgeon to make sure the patient's asthma is under excellent control, prior to submitting a waiver application.

Table 1: Waiver notential for asthma and EIR

| Flying  | ver potential for asthma and Ell Condition/Treatment | Waiver Potential | ACS evaluation |
|---------|--|------------------|----------------|
| Class   | 3333===================================              | Waiver Authority | required       |
| I/IA    | History of childhood asthma                          | Yes              | No             |
|         | ≤12 (before 13 <sup>th</sup> birthday)               | AETC             |                |
|         | History of asthma after age 12                       | No               | No             |
|         | (≥13) and/or asthma/exercise-                        | AETC             |                |
|         | induced bronchospasm controlled on any medication    |                  |                |
| II/III  | Initial FC II, history of                            | Yes              | No             |
| SWA     | childhood asthma ≤12-years-                          | AETC             |                |
|         | old  |                  |                |
|         |  | No               | No             |
|         | Initial FC II, history of                            | AETC             |                |
|         | childhood asthma ≥13-years-                          | Yes **#          | V + 0-         |
|         | old  | AFMRA            | Yes†&          |
|         | Any active asthma history*                           | ATWIKA           |                |
|         | I my detive asamia mistory                           | No               | No             |
|         |  | AFMRA            |                |
|         | Asthma treated with beta-                            |                  |                |
|         | agonists‡, theophylline,                             |                  |                |
|         | systemic corticosteroids                             |                  |                |
| ATC/GBO | Initial, history of childhood                        | Yes              | No             |
|         | asthma ≤12-years-old                                 | AFMRA            |                |
|         | Initial, history of childhood                        | No               | No             |
|         | asthma ≥13-years-old                                 | AFMRA            |                |
|         | exercise-induced                                     | Yes              | No             |
|         | bronchospasm (prophylaxed                            | AFMRA            |                |
|         | with albuterol*)                                     |                  |                |
|         | Any active asthma history*                           | Yes              | No             |
|         |  | AFMRA            |                |
|         | Asthma treated with                                  | No               | No             |
|         | theophylline, systemic                               | AFMRA            |                |
|         | corticosteroids                                      |                  |                |

<sup>\*</sup> Use of more than three metered-dose SABA inhalers per year is suspicious for utilization as rescue treatment.
† ACS evaluation will normally include methacholine challenge testing and possibly exercise challenge to assess sufficiency of therapy.

<sup>#</sup> For FC II waiver may be considered with AFMRA being the waiver authority.

<sup>&</sup>amp; ACS evaluations for FC II personnel only.

A review of AIMWTS in Jul 2015 revealed 1416 cases of asthma or a history of asthma. There were 356 cases resulting in a disqualified disposition. Breakdown of the cases revealed 428 FC I/IA cases, 249 FC II cases, 500 FC III cases, 143 ATC/GBC cases, and 96 MOD cases. Of the 356 asthma cases disqualified, 100 were FCI/IA, 48 were FC II, 158 were FC III, 29 were ATC/GBC and 19 were MOD. In the disqualified category, about 80% were disqualified for the asthma [e.g. controlled on previously non-waiverable medications (Advair®, albuterol), not well controlled, childhood asthma after age 12] and the others were disqualified for other medical conditions.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for exercised induced bronchospasm (EIB) should include:

- A. Detailed chronology of asthmatic episodes, provocative factors, emergency room visits and treatment.
- B. Rate of utilization of metered-dose inhalers.
- C. Results of all spirometry studies (FEV1, FVC, and FEV/FEC) (Note 1).
- D. Internal medicine, pulmonary consult or allergy consult.
- E. Medical evaluation board (MEB) results.

<u>Note 1</u>:. At least one study should include post-bronchodilator spirometry, regardless of whether baseline spirometry is "within normal limits." In individuals with suspected EIB, exercise challenge testing should be performed to establish the diagnosis.

The aeromedical summary for asthma should include:

- A. Detailed chronology of asthmatic episodes, provocative factors, current Asthma Control Test score (Note 4), emergency room visits and treatment.
- B. Results of all spirometry. Should also include results of spirometry with pre and post bronchodilator after three months on current therapy [ICS (Note 2) +/- LABA, montelukast (possibly cromolyn)].
- C. Internal medicine or pulmonary consult.
- D. Allergy consult if individual also has allergic rhinitis.
- E. MEB results, if complete.
- <u>Note 2</u>: The choice of ICS is probably irrelevant, though some research suggests fluticasone may cause more HPA axis suppression on an equipotent dose compared with budesonide and others. Regardless of the ICS used, it is important to use the lowest dose necessary to achieve control.
- <u>Note 3</u>: Bronchoprovocation is <u>not</u> recommended as part of the waiver submission process, ACS may accomplish testing during ACS evaluation.
- Note 4: The Asthma Control Test (ACT) is a quick, 5 question assessment tool that is meant to quantify the level of the patient's asthma control. It is scored on a scale of 5-25. The American

Thoracic Society considers a score of > 19 to be indicative of well-controlled asthma. The questionnaire can be found at www.asthmacontroltest.com.

### III. Overview.

Although it is unlikely that asthma has ever been a rare disorder, over the past twenty years the prevalence has increased by roughly 40%. Numerous hypotheses have been advanced to explain the rise in prevalence, such as decreased air exchange in energy-efficient buildings, or decreased childhood infections resulting in an upregulation of IgE-mediated immunity, but no consensus exists. Given the fact that asthma as a cause of death is rarely confused with any other etiology, and the fact that the increase in prevalence has been documented in numerous countries, the increase in prevalence is unlikely to be an artifact of inconsistent diagnostic criteria.<sup>2-5</sup>

That being said, variations in diagnostic criteria do affect epidemiologic studies of asthma. For such a common disease, it has been surprisingly difficult to agree on a definition. In clinical practice, inconsistent criteria have resulted in a great deal of variability in applying the diagnosis. Asthma has also had more than its share of euphemistic alternative names, including reactive airways disease, reactive bronchitis, and others. Asthma is a chronic disorder of the airways that is complex and characterized by variable and recurring airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation. The interaction of these features of asthma determines the clinical manifestations, the severity of asthma and the response to treatment. Excluded from this definition would be airway inflammation that complicates other structural lung diseases, or that results from serious insults, such as toxins or significant infections (e.g., smoke inhalation, industrial accidents, influenza). The qualification that the infection should be significant is important, albeit difficult to delimit. To give an example, six weeks of persistent cough following a common rhinovirus infection should raise a suspicion for asthma, and if this is a recurring pattern, the diagnosis is probable. Prolonged symptoms after viral infection are considerably more common in children, as discussed below.

With the understanding that diagnostic criteria vary, current asthma prevalence is estimated to be 8.2% of the U.S. population (24.6 million people); within population subgroups it tends to be higher among females, children, persons of non-Hispanic black and Puerto Rican ethnicity, persons with family income below the poverty level, and those residing in the Northeast and Midwest regions of the U.S.<sup>7</sup> Consideration of secondary etiologic factors is important, since mitigation of those factors may allow better or (rarely) complete control. Asthma often shows an atopic association, particularly with allergic rhinitis, and treatment of allergic rhinitis with immunotherapy may lead to marked improvement in asthmatic symptoms. In the absence of allergic rhinitis, immunotherapy in an attempt to directly control asthma is rarely of value. Avoidance of allergens would seem to be an obvious recommendation in atopic cases, but this is rarely practical, particularly in military environments. On occasion, a specific avoidable precipitating factor is identified by history or skin testing, and can be successfully avoided. Animal, particularly cat, allergy is the most common example whereby avoidance may succeed in controlling asthma. Chronic rhinitis may be accompanied by sinusitis and, anecdotally, treatment of chronic sinusitis has occasionally resulted in better control of asthma. There is also an association of asthma with gastroesophageal reflux, but it is unclear which is cause and which is effect, since pressure excursions within the thorax and abdomen may predispose to reflux.

Acid suppression with proton pump inhibitors rarely leads to clinical improvement, and most reviews have failed to support a role for reflux in asthma pathogenesis. However, in rare instances, reflux with nocturnal aspiration of gastric secretions may mimic asthma. As opposed to etiologic factors, exacerbating factors are often easy to identify; while these may be idiosyncratic to the individual, attacks are commonly precipitated by exercise in cold, dry air, by exposure to pollutants (e.g., exhaust fumes), or by viral respiratory infections.

Exacerbation of chronic or intermittent asthma by exercise is an extremely common symptom, reported by 70-90% of asthmatics; since it is well documented that many individuals fail to symptomatically differentiate asthma from normal exertional breathlessness, even this percentage may be an underestimate.<sup>8,9</sup> In addition to exercise exacerbating bronchospasm in established asthma, there is a separate phenomenon of solitary exercise-induced bronchospasm (EIB). Unfortunately, published reports of EIB often fail to separate the two conditions, making interpretation of results difficult in those studies. Solitary EIB appears to be due to airway hyperosmolarity induced by hyperpnea and free water loss, and/or cooling and subsequent rewarming of the airways. There are no published reports of death from solitary EIB. In contrast, asthmatic deaths as a result of exercise in those with established asthma are well documented.<sup>10</sup> Solitary EIB occurs in recreational as well as high school and collegiate athletes; the prevalence is significant, typically affecting about 9-12% of children in athletic programs. 11 This percentage is based on results of post-exercise spirometry; many did not have significant symptoms. The phenomenon has been best studied in professional athletes. Endurance sports have a higher risk than intermittent activities. Among cross-country runners in one study, 14% of those without a history of asthma showed objective evidence of EIB.<sup>9</sup> The greatest risk involves winter sports, which is consistent with the likely mechanism of EIB. Screening of the 1998 Winter Olympic Team using sport-specific challenge showed an overall rate of EIB of 23%, with cross-country skiing showing a prevalence of 50%. Another study found a 35% prevalence of solitary EIB in figure skaters. <sup>12</sup> Unlike the case in established asthma, inflammation is generally not believed to play a role in solitary EIB, though endurance athletes in winter sports may actually show inflammatory changes on histopathology. 13

The major symptoms of asthma include wheezing, shortness of breath, chest tightness, and cough. Both clinical experience and studies have shown that subjective reporting of symptoms does not correlate well with severity of obstruction. Patients tend to adapt to chronic airflow obstruction, so that symptoms correlate better with the rate of fall of FEV1 during an attack, rather than with the absolute degree of obstruction. Spirometry utilizing the forced vital capacity maneuver is the standard method for measuring obstruction. Proper technique and adequate effort by the individual are crucial. In the past, a ratio of FEV1/FVC less than 0.75 was used to define the presence of airflow obstruction. However, the normal range of FEV1 can vary significantly, depending on race, age, gender, and anthropomorphic measurements. Population based studies of normal individuals have been used to create algorithms that take these factors into account. By convention, we consider values above the 95th or below the 5th percentile for a given population to be abnormal. Modern pulmonary function testing equipment utilizes these algorithms to predict a normal range for spirometric testing. Airway obstruction is defined as a FEV1/FVC ratio lower than the predicted range for the individual patient. The FEV1 is used to gauge the severity of the obstruction. Reversible airway obstruction is defined as an increase of at least 12% and 200 mL in FEV1 and/or FVC, after administration of an inhaled bronchodilator.

A 12% relative and 200 mL absolute change in FEV1 over time (an interval that may be anywhere from minutes to months) should also raise suspicion that a reversible obstruction may be present. A post-bronchodilator study may also be useful in those with low-normal airflows who have a suspicious history; even if the FEV1/FVC falls within the normal range, a 12% and 200 mL improvement in FEV1 indicates reversible obstruction. Whether the finding of reversible obstruction signifies asthma, depends on the clinical setting. Bronchospasm may complicate airway inflammation from any of a number of etiologies. Serious respiratory infections such as influenza are often accompanied by airway inflammation that may persist for weeks, and the presence of reversible airflow obstruction during this period would not equate to asthma. Airflow obstruction is often a feature of other chronic diseases involving the airways (e.g., chronic obstructive pulmonary disease [COPD], bronchiectasis), and when the obstructive pathophysiology involves inflammation, the airflow obstruction may be at least partially reversible.

Children are prone to asthma. As many as a third will have symptoms compatible with asthma at some point, most often in the early pre-school years. Some of these cases represent a prolonged response to viral bronchiolitis, in particular from respiratory syncytial virus. This is especially true in infancy. The longer that symptoms persist, the more likely that the problem truly represents asthma. For childhood asthma, age shows a clear association with asthma prevalence. In the British 1958 cohort, of 880 subjects with asthma during preschool years, 50% still wheezed at age 7, 18% at age 11, 10% at ages 16 and 23.<sup>14</sup>

Selection of aircrew for military aviation is complicated by the fact that many asthmatics who become free of symptoms in early adolescence will suffer relapse in their twenties or early thirties. In the British 1958 study noted earlier, after reaching a nadir in late adolescence and the early twenties, the percentage of those with active wheezing rose to 27% by age 33. In general, about 30-35% of remitted childhood asthmatics will relapse. Numerous natural history studies have attempted to correlate a variety of factors (e.g., childhood pet exposure) to the risk of persistence or relapse of asthma, but results have been contradictory. Cofactors that have correlated in reasonably consistent fashion to the risk of relapse have included a history of atopy and the frequency and severity of attacks in childhood, but since the risk of relapse is only about one and a half times the background risk, neither factor is a particularly useful predictor. Furthermore, even when pediatric medical records are reasonably complete, it is surprisingly difficult except in the most severe cases to quantify frequency or severity of childhood asthma. Remission at a very early age is associated with less risk of subsequent asthma, in that those with wheezing confined to infancy, i.e., less than two years old, have been shown to be at no greater risk of adult relapse than those who never wheezed. 15

A number of studies have shown that airway inflammation and/or hyperreactivity frequently persist in adolescents who have clinically remitted. Regardless of whether disease activity has been measured by elevated eosinophils in bronchoalveolar lavage, abnormal endobronchial histopathology, or positive methacholine challenge testing, anywhere from a quarter to two-thirds of those in apparent remission have evidence of continued subclinical activity. Not unreasonably, this has led to a perception that bronchoprovocation testing of individuals in remission could identify those at greater risk of later relapse. Reasonable or not, the perception has proven to be incorrect. The prevalence of methacholine reactivity from childhood to

adulthood has been shown to simply mirror the prevalence of asthma; many of those who show normal reactivity in their early twenties show a recurrence of reactivity at a later age. <sup>18</sup> A study of allergic rhinitis patients showed no difference in the risk of developing asthma between those with positive and negative bronchoprovocation tests. <sup>19</sup> Most convincingly, in a publication from the data in the Dunedin (New Zealand) cohort, of 58 subjects in their mid-teens with remission of childhood asthma and negative methacholine challenge testing, 33% subsequently relapsed by age 26, consistent with historical rates of relapse. <sup>20</sup> Those with positive bronchoprovocation testing showed a slightly greater risk of relapse, but that group numbered only six individuals, of whom three relapsed. Broncho-provocation testing appears to be of no value in predicting relapse in remitted childhood asthmatics.

Medications employed to treat asthma are generally classified as controller, rescue, or, in the case of EIB, prophylactic therapy.<sup>21</sup> Rescue therapy primarily consists of a variety of shortacting beta-agonists (SABA) delivered via inhalation. In addition to the fact that these agents have a number of cardiac and neurologic adverse effects, the need for a SABA generally signifies asthma that is not under control. However, prophylactic use prior to exercising in those with solitary EIB does not indicate a similar lack of control, and within certain limits outlined below, such use is waiverable. Use of albuterol fifteen minutes before exertion generally confers protection for about four hours. Among controller medications, inhaled corticosteroids (ICS) are the mainstay of asthma therapy. They have been shown to control disease and reduce the number of exacerbations. It is very important that patients understand that these are slow-acting medications; while some benefit is apparent as early as a week or two, continued improvement may be seen for up to twelve months. Adverse effects are usually local, consisting of pharyngeal candidiasis (thrush), which is generally avoidable by rinsing and gargling after inhalation, and a smaller risk of dysphonia. At high doses, some suppression of the hypothalamic-pituitaryadrenal (HPA) axis may occur, though this is rare. Leukotriene modifiers (leukotriene receptor antagonist), including montelukast (Singulair® and Montelo-10®), zafirlukast (Accolate®) and zileutin (Zyflo®) have very few adverse effects, though they are generally less effective than inhaled steroids. Nonetheless, some patients respond well, and it can be useful as add-on therapy, or to allow reduction of the inhaled steroid. It reaches maximal effect within about a day of therapy, and doses higher than 10 mg are of no additional value. Cromolyn sodium is nearly devoid of adverse effects, but is rarely efficacious in adults.<sup>22</sup>

Other medications are not compatible with USAF aviation. Long-acting beta-agonists (LABA) such as salmeterol (Serevent®, contained in Advair®), formoterol (Foradil®, contained in Symbicort® and Dulera®), vilanterol (contained in Breo® Ellipta and Anoro®), olodaterol (Striverdi®), and indacaterol (Arcepta®) have been in vogue in recent years. They are generally classified as controllers, though suppressor is a better term, since they fail to address the underlying inflammatory process. Administering a LABA twice a day differs little, if at all, from plying a patient every four hours with a SABA and are not to be used as monotherapy for long-term asthma control. As with SABAs, tolerance with LABAs is a real problem, and concerns about cardiac and neurologic adverse effects are similar. The tolerance problem is best illustrated with EIB; not only does regular use of a SABA or LABA result in less prophylactic efficacy prior to exercise, and a sluggish response to rescue bronchodilation, but such use also typically results in the occurrence of more severe EIB. Furthermore, prospective data have shown use of salmeterol is associated with increased mortality, echoing the experience with

isoproterenol and fenoterol in previous decades. For this reason, the U.S. Food and Drug Administration (FDA) has published an advisory, and salmeterol is not recommended as first-line therapy.<sup>22</sup> The possible mechanisms behind the increase in asthma mortality with salmeterol are direct toxicity, tolerance, delay in seeking help, and decreased use of inhaled corticosteroids.<sup>23</sup> While the study cited was performed using salmeterol, there is little reason to assume other LABAs would be any different. In fact, FDA now requires a black box warning for all drugs in this class, warning against the risks of asthma-related death.

A second class of long acting bronchodilators, known as long acting muscarinic antagonists (LAMAs), has traditionally been used to treat COPD. Drugs in this class include tiotropium (Spiriva®), aclidinium bromide (Tudorza Pressair®), and umeclidinium (contained in Anoro®). In 2010, a study published in the New England Journal of Medicine suggested that tiotropium could be useful for the treatment of asthma that was incompletely controlled with inhaled corticosteroids. Since then, numerous studies have been published, confirming the efficacy of tiotropium as step-up therapy for poorly controlled asthma. Based on this, tiotropium now has an indication for the treatment of asthma in Europe. While the manufacturer has applied to the FDA for an indication in the treatment of asthma, its utilization in this capacity currently constitutes off-label use. Furthermore, most of the aeromedical concerns regarding LABAs also apply to the use of LAMAs. For these reasons, the use of LAMAs is not waiverable.

Theophylline has a very narrow therapeutic window, and is associated with highly significant adverse effects, such as cardiac arrhythmias and seizures. Systemic steroid therapy is complicated by serious adverse effects with either acute or chronic use, and within a few weeks of therapy the HPA axis is effectively suppressed. Furthermore, the fact that the individual needs systemic steroid therapy denotes a severe degree of asthma.

## IV. Aeromedical Concerns.

Severity of obstruction and presence/absence of symptoms are clearly important, but the principal aeromedical concern is the risk of serious bronchospasm in response to minor insults. Since breathing cold, dry air, or exposure to smoke, fumes or pressure breathing can provoke asthma attacks; the danger of incapacitating bronchospasm is real. In particular, exercise in cold, dry air is one of the most consistent provocative stimuli, whether for established asthma or for solitary EIB. Thus, high-performance aviation is not recommended for either condition. Additionally, military aviation concerns include lack of available care in austere locations. This typically results in deployability restrictions.

| ICD-9 Codes for Asthma |  |  |
|------------------------|--|--|
| 493.0                  | Extrinsic asthma   |  |
| 493.1                  | Intrinsic asthma   |  |
| 493.2                  | Chronic obstructive asthma                               |  |
| 493.3                  | Other forms of asthma (exercised induced, cough variant) |  |
| 493.9                  | Asthma, unspecified                                      |  |

| ICD-10 Codes for Asthma |   |  |
|-------------------------|---|--|
| J45.20                  | Mild intermittent asthma, uncomplicated |  |
| J45.998                 | Other asthma                            |  |
| 493.9                   | Unspecified asthma, uncomplicated       |  |

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#### **WAIVER GUIDE**

Updated: Feb 2015

Supersedes waiver guide of Aug 2011

By: Lt Col Tory Woodard (RAM 16), Dr. Dan Van Syoc, Lt Col Steven Gore, and Maj Eddie

Davenport (ACS Chief Cardiologist)

### **CONDITION:**

**Atrial Fibrillation & Atrial Flutter (Feb 2015)** 

### I. Waiver Considerations.

History of AF and/or atrial flutter is disqualifying for all flying classes. For retention purposes, any type of atrial fibrillation or atrial flutter is disqualifying. The one exception is a single episode of atrial fibrillation clearly associated with a reversible cause. Additionally, the use of maintenance medications for the treatment or prevention of major rhythm disturbances including atrial flutter or atrial fibrillation requires a waiver for retention and all flying classes. A history of catheter ablation is also disqualifying for all flying classes and is addressed in a separate waiver guide; Radiofrequency Ablation (RFA) of Tachyarrhythmias. If hyperthyroidism is determined to be the cause of the AF, a waiver may be considered per policy after correction of the hyperthyroidism (the hyperthyroidism waiver guide needs to be considered in those cases).

Table 1: Atrial fibrillation (lone), atrial flutter and waiver potential.@

| Flying           | Condition  | Waiver Potential   | ACS               |
|------------------|--|--------------------|-------------------|
| Class            |  | Waiver Authority   | Review/Evaluation |
| I/IA             | Atrial fibrillation, single episode, without hemodynamic symptoms, no medications, and including "holiday heart" scenario.   | Maybe†<br>AETC     | Yes               |
|                  | All other <u>atrial fibrillation</u> episodes, with or without hemodynamic symptoms.   | No<br>AETC         | No                |
|                  | Atrial flutter, with or without hemodynamic symptoms.  | No<br>AETC         | No                |
| II/III**         | Atrial fibrillation, single episode, without hemodynamic symptoms, no medications.   | Yes†\$*<br>MAJCOM& | Yes               |
|                  | Atrial flutter with successful radiofrequency ablation and/or atrial fibrillation, paroxysmal or chronic, without hemodynamic symptoms, with or without beta-blocker, with or without radiofrequency ablation. | Maybe#+\$<br>AFMRA | Yes               |
|                  | Atrial flutter, without successful radiofrequency ablation and/or atrial fibrillation with hemodynamic symptoms.   | No<br>MAJCOM       | No                |
| ATC/GBO<br>SWA** | Atrial fibrillation (unless single episode with identified reversible cause, without hemodynamic symptoms, no maintenance medications OR unless successfully ablated). ‡                                       | Maybe†<br>AFMSA    | No                |
|                  | Atrial flutter, (unless successful radiofrequency ablation).**   | Maybe<br>AFMRA     | No                |

<sup>†</sup> Waiver for single episode AF should not be submitted until at least 3 months after conversion to sinus rhythm, including a minimum of two months off antiarrhythmic medications. There is a minimum 3 months observation before submitting waiver for paroxysmal and chronic atrial fibrillation.

- \$ For untrained FC II individuals waiver is unlikely and for untrained FC III individuals waiver will be considered on a case by case basis.
- # In cases of paroxysmal and chronic atrial fibrillation treated with or without beta-blocker, waiver will be restricted to low performance aircraft (IIA) and in case of pilots, with another qualified pilot at redundant controls (IIC).
- + If treated with radiofrequency ablation, see *Radiofrequency Ablation (RFA) of Tachyarrhythmias* waiver guide for further guidance.
- \* In cases of paroxysmal and chronic atrial fibrillation treated with or without beta-blocker, FC III individuals are restricted to low performance aircraft.
- & Atrial flutter, single occurrence, without structural cardiac abnormality and/or related to acute alcohol and/or stimulant intake, may be waiverable WITH ACS evaluation
- \*\* Initial FC II/III waiver authority is AETC.
- @ Per AFI 48-123 6.4.1.3, AFMRA remains waiver authority for all initial waivers for conditions that do not meet retention standards, unless 6.4.1.4.1 applies.
- ‡If individual meets all "unless" criteria for their diagnosis, then they meet the standard for ATC/GBO/SWA. If they do not meet the "unless" criteria, an MEB is required and AFMRA retains waiver authority.

Review of AIMWTS through Feb 2015 revealed 200 cases of atrial fibrillation/flutter; there were 28 disqualified cases. Breakdown of the cases revealed: 3 FC I/A cases (1 disqualified), 121 FC II cases (17 disqualified), 63 FC III cases (9 disqualified), and 5 ATC/GBC cases (0 disqualified), and 8 MOD cases (1 disqualified).

# II. Information Required for Waiver Submission.

Aeromedical disposition and waiver submission should only be submitted after administrative and clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for <u>initial waiver</u> for single episode of atrial fibrillation converted to sinus rhythm should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, blood pressure, medications, and activity level.
- B. Cardiology consult.
- C. Electrocardiogram (ECG) during atrial fibrillation and after conversion to sinus rhythm.
- D. Report and videotape/CD copy of echocardiogram to the ACS, study performed after conversion to sinus rhythm. (Notes 1 and 2)
- E. Lab testing to include Complete Blood Count (CBC), Complete Metabolic Panel (CMP) and Thyroid function test (TSH).
- F. Report and representative tracings of Holter monitor performed in the final month of DNIF observation.
- G. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (See notes 1 and 2)
- H. Results of medical evaluation board MEB (worldwide duty evaluation for ARC members), if required.

The aeromedical summary for <u>initial waiver</u> for paroxysmal or chronic atrial fibrillation or atrial flutter should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, blood pressure, medications, and activity level.
- B. Cardiology consult.
- C. Electrocardiogram (ECG).
- D. Report and videotape/CD copy of echocardiogram to the ACS. (Notes 1 and 2)
- E. Lab testing to include Complete Blood Count (CBC), Complete Metabolic Panel (CMP) and Thyroid function test (TSH).
- F. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (See notes 1 and 2)
- G. Results of medical evaluation board MEB (worldwide duty evaluation for ARC members), if required.

The aeromedical summary <u>for waiver renewal</u> should contain the following information:

A. Complete history and physical exam – to include description of any symptoms, medications, and activity level.

B. Electrocardiogram (ECG).

C. Additional local cardiac testing is not routinely required for re-evaluation cases followed at the ACS but may be requested in individual cases. If so, the previous ACS evaluation/review will specify details regarding any requested local testing.

D. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (See notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM)

USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia. Its prevalence is 0.4-1% in the general U.S. population, although values of 1.5-2.9% have been reported in European studies. A 2012 study of United Kingdom aircrew found asymptomatic atrial fibrillation in 0.3% of patients screened during routine ECG screening. Risk factors for AF include alcohol abuse, stress, smoking, excessive caffeine intake, drugs, hyperthyroidism, acute diarrhea, respiratory disease, excessive physical activity and fatigue or exhaustion. The frequency of AF increases with age, and can be complicated by thromboembolic events, palpitations, heart failure and syncope. These complications may expose aircrew to risks which could be detrimental to flight safety. The aeromedical disposition of atrial fibrillation with other associated comorbidities should be guided by policies for the underlying comorbid conditions (e.g., hypertension, hyperthyroidism, congestive heart failure, valvular heart disease, and cardiomyopathy) and the AF considered a complication or endpoint. This waiver guide addresses lone AF, a misleading term in the cardiac literature, which would be better termed idiopathic AF. Lone (or idiopathic) AF is defined as AF without structural heart disease, hyperthyroidism or hypertension in patients under age 60 at presentation. Lone AF may occur as a single isolated episode, recurrent paroxysmal events or chronically persistent AF. AF encountered in the military aircrew population will usually be lone AF that is converted spontaneously or by medical intervention within 24 hours. A single idiopathic episode often has an identifiable precipitating cause, such as acute abuse of alcohol (holiday heart syndrome) and/or other stimulant use (heavy caffeine and decongestant use, weight lifting supplements, illicit drug use, etc.) By definition Lone AF (even if persistent or permanent) is at low risk for thromboembolism, thus any risk score used to determine thromboembolic / CVA risk such as the CHADS2 or a CHA2DS2-VASc score should

be "0" and thus anticoagulation not recommended. If an aviator meets anticoagulation criteria then stroke risk is over 1% and thus permanent disqualification is recommended.

Atrial flutter is often associated with atrial fibrillation and has similar risks of tachycardia and thromboembolism. While atrial flutter may be a complication of underlying cardiac disease (36%-76% in reviewed studies), this waiver guide addresses idiopathic atrial flutter not associated with an underlying disease. The atrial rate of atrial flutter is commonly around 300 beats per minute. Typically there is physiologic AV block of 4:1, 3:1 or 2:1, yielding a ventricular rate of about 75, 100 or 150 beats per minute, respectively. However, 1:1 conduction with a ventricular rate of about 300 beats per minute is possible, especially in young and healthy subjects. Given expected resting ventricular rates up to 150 beats per minute, persistent or frequent atrial flutter thus may require AV node blocking medication for ventricular rate control.

Initial treatment of AF or atrial flutter depends on the individual's clinical status, but the major objective is to slow the ventricular rate and/or restore sinus rhythm. Medications and/or cardioversion may be used. In cases of lone AF, one month of prophylactic therapy with beta blocker, calcium channel blocker or digitalis preparation may be used after sinus rhythm is restored to suppress short-term recurrence of AF. A history of cardioversion or short-term use of antiarrhythmic medications or anticoagulation does not preclude waiver and should not delay waiver processing.

Medications and/or radiofrequency ablation are used for long term management of paroxysmal and chronic AF and atrial flutter. Paroxysmal and chronic AF often require chronic treatment with an atrioventricular (AV) node blocking medication, such as a beta blocker, nondihydropyridine calcium channel blocker or digitalis for ventricular rate control. The betablockers atenolol and metoprolol are the only AV node blocking agents currently approved for aircrew. Dihydropyridine calcium channel blockers currently approved to treat hypertension in aircrew (such as Procardia XL® and Adalat CC®) are not effective for AV node blockade. Atrial flutter can also be treated with AV node blocking medication, but control is often difficult to achieve. Both AF and atrial flutter may also be treated by radiofrequency ablation. Ablation of atrial flutter is very low risk, technically simple, and has a greater than 90% success rate. Radiofrequency ablation for AF is 70 to 85% effective in individuals with paroxysmal AF and 50 to 70% in individuals with chronic AF. Repeat ablations do carry higher success rates. Only 1.2% of those treated for paroxysmal AF have been shown to progress to persistent AF in shortterm follow-up studies, with a progression rate of only 0.3% per year. Aeromedical guidelines for ablation of AF and atrial flutter are discussed in a separate waiver guide, Radiofrequency Ablation (RFA) of Tachyarrhythmias.

#### IV. Aeromedical Concerns.

Clinical and aeromedical concerns for lone AF and atrial flutter include hemodynamic instability and exercise intolerance, thromboembolic risk and a requirement for chronic medication use to maintain sinus rhythm or to control ventricular rate. The loss of atrial contribution to cardiac output, loss of atrioventricular synchrony, and a rapid ventricular rate response during an afib/flutter episode may impair cardiac performance, especially during exertion, resulting in hemodynamic symptoms or reduced exercise capacity. This reduced exercise capacity has

operational implications, especially for pilots in high performance aircraft. AV node blocking medication may be required – and without such use, the ventricular rate response of AF during exertion may quickly increase to the range of 220-250 beats per minute. Published guidelines regarding the management of AF recommend that beta-blockers are safe and effective for long-term control of ventricular rate response at rest and during exercise. However, AV node blockade with beta-blocker use suppresses heart rate and blood pressure response, creating an aeromedical concern regarding +Gz tolerance.

Clinical literature typically reports cardiac event rates less than 1% per year for lone AF, whether a single event, paroxysmal or chronic in mechanism. Previously, waivers for AF were limited to an isolated episode without hemodynamic symptoms. In an attempt to better define the natural history of lone AF in this young and otherwise healthy population and to refine waiver policy, the Aeromedical Consultation Service (ACS) reviewed its experience with AF in aircrew. From 1957 to 1993, 300 male aircrew were evaluated for AF approximately 6 months after the initial AF episode. Two hundred thirty-four of the 300 (78%) were found to have lone AF. The events considered were hemodynamic symptoms, cerebral ischemic events, and sudden cardiac death. The arrhythmic event rate prior to age 60 was low (0.4% per year) and the likelihood of a cerebral ischemic event before age 60 without chronic AF was minimal (none in this review). In those initially presenting with an isolated episode of AF, 63% had no recurrence, 36% developed paroxysmal AF and 1% developed chronic AF. In those presenting initially with paroxysmal AF, 15% subsequently developed chronic AF.

| ICD-9 Codes for atrial fibrillation and flutter |                     |  |
|---|---------------------|--|
| 427.31  | Atrial fibrillation |  |
| 427.32 Atrial flutter                           |                     |  |

| ICD-10 Codes for atrial fibrillation and flutter |                                 |
|--|---------------------------------|
| I48.91   | Unspecified Atrial fibrillation |
| I48.82 Unspecified Atrial flutter                |                                 |

#### V. References.

- 1. Boos CJ, Jamil Y, Park M, et al. Electrocardiographic Abnormalities in Medically Screened Military Aircrew. Aviat Space Environ Med, 2012; 83: 1055-59.
- 2. Brembilla-Perrot B, Laporte F, Sellal JM, et al. 1:1 atrial flutter. Prevalence and clinical characteristics. Int J Cardiol, 2013; 168(4): 3287-90.
- 3. Friberg L and Bergfeldt L. Atrial fibrillation prevalence revisited. J Intern Med, 2013; 274(5): 461-68.
- 4. Kruyer WB and Davenport ED. Cardiology. Ch. 2 in: *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., Castle Connolly Graduate Medical Publishing, LTD, 2013; 75-79.

- 5. Luria DM, Hodge DO, Monahan KH, et. al. Effect of Radiofrequency Ablation of Atrial Flutter on the Natural History of Subsequent Atrial Arrhythmias. J Cardiovasc Electrophysiol, 2008; 19(11): 1145-50.
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- 7. Morady F and Zipes DP. Atrial Fibrillation: Clinical Features, Mechanisms, and Management, Ch. 38 in *Mann: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 10<sup>th</sup> ed., Saunders, 2014.
- 8. Ozturk C, Aparci M, Cakmak T, et al. Atrial Fibrillation Presented with Syncope in a Jet Pilot During Daily Briefing on Squadron. Aviat Space Environ Med, 2014; 85: 965-69.
- 9. Strader JR, Jr, Gray GW, Kruyer WB. Clinical Aerospace Cardiovascular Medicine. Ch. 13 in: *Fundamentals of Aerospace Medicine*, 4<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins, 2008; 344-45.
- 10. Takigawa M, Takahashi A, Kuwahara T, et al. Long Term Follow-Up After Catheter Ablation of Paroxysmal Atrial Fibrillation: The Incidence of Recurrence and Progression of Atrial Fibrillation. Circulation: Arrhythm Electrophysiol, 2014; 7: 267-73

#### **WAIVER GUIDE**

Updated: Sep 2015

Supersedes waiver guide of Sep 2011

By: Dr. Kevin Van Valkenburg (RAM 16) and Dr. Dan Van Syoc Reviewed by Lt Col Eddie Davenport, Chief ACS Cardiologist

### **CONDITION:**

**Atrioventricular Conduction Disturbances (Sep 2015)** 

#### I. Waiver Considerations.

As noted below, first degree AV block and Mobitz I second-degree AV block are generally considered normal variants and as such do not require a waiver. Mobitz II second degree block and third degree block are disqualifying for all classes. If further testing is requested by the ACS ECG Library for unusual individual cases, aeromedical disposition will be guided by the findings. Since these are normally incidental findings on routine ECGs, DNIF of the aircrew member is not required for further work-up unless specifically recommended by the ACS. Few aviators with Mobitz II second degree AV block or third degree AV block are seen at the ACS because the recommendation for permanent cardiac pacing and the risk of hemodynamic symptoms is not compatible with flying status. Waiver for these two diagnoses is unlikely. For ATC/GBO/SWA personnel, retention standards state that symptomatic or asymptomatic second degree Type II or third degree atrioventricular block, or symptomatic second degree Type I atrioventricular block are disqualifying. The exception is atrioventricular blocks, which are clearly associated with a reversible cause.

Table 1: Waiver potential for AV conduction disturbances.

| Flying Class   | Condition                 | Waiver Potential | ACS                   |
|----------------|---------------------------|------------------|-----------------------|
|                |                           | Waiver Authority | Review/Evaluation     |
| I/IA           | First degree AV block and | Not required -   | Yes#                  |
|                | Mobitz I second degree    | qualified        |                       |
|                | AV block (Wenckebach)     |                  |                       |
|                | Mobitz II second degree   |                  |                       |
|                | AV block and third degree | No               | Yes#                  |
|                | (complete) block          | AETC             |                       |
| II, including  | First degree AV block and | Not required -   | Yes*                  |
| untrained      | Mobitz I second degree    | qualified        |                       |
|                | AV block (Wenckebach)     |                  |                       |
|                | Mobitz II second degree   |                  |                       |
|                | AV block and third degree | No               | Yes*                  |
|                | (complete) block          | AFMRA            |                       |
| III, including | First degree AV block and | Not required -   | No (certifying        |
| untrained      | Mobitz I second degree    | qualified        | authority for initial |
|                | AV block (Wenckebach)     |                  | physicals may send    |
|                |                           |                  | to ECG Library)       |
|                | Mobitz II second degree   |                  |                       |
|                | AV block and third degree | No               | Yes                   |
|                | (complete) block          | AFMRA            |                       |
| ATC/GBO        | First degree AV block and | Not required -   | No                    |
| SWA            | Mobitz I second degree    | qualified        |                       |
|                | AV block (Wenckebach)     |                  |                       |
|                |                           |                  |                       |
|                | Mobitz II second degree   |                  | No                    |
|                | AV block and third degree | No               |                       |
|                | (complete) block          | AFMRA            |                       |

<sup>#</sup> ECG Library is reviewing all FC I/IA ECGs (USAFA, USAFSAM and AD sent by HQ AETC).

A review of AIMWTS in Jun 2015 revealed 35 cases of AV conduction disturbances: 4 FC I/IA, 13 FC II (2 disqualifications), 16 FC III (2 disqualifications), and 2 ATC/GBC. Two of the disqualified cases were for Mobitz type II, one for multiple medical problems and one for vision-related issues. Many of the cases granted waiver were for first-degree AV block or Mobitz I second degree AV block, which is no longer required.

<sup>\*</sup> ECG Library would review; all cardiac studies on FC II individuals are required to be sent to ECG library for review.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary should contain the following information for waiver for Mobitz II second degree block, third degree (complete) block or if ECG library identifies abnormal first degree block or Mobitz I second degree block requiring waiver:

A. Complete history and physical exam – to include description of symptoms (negative included), medications/treatment, and activity level.

B. Cardiology consult. (Not required in abnormal first degree block or Mobitz I second degree block, if ECG library does not request.)

C. Electrocardiogram (ECG).

D. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)

E. MEB results.

Note 1: The address to send tracings, CDs, and reports if not uploaded electronically:

Attn: Case Manager for (patient's MAJCOM)

USAFSAM/FECI

Facility 20840

2510 Fifth Street

WPAFB, OH 45433-7913

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

Atrioventricular (AV) conduction disturbances include first degree AV block, Mobitz I second degree AV block (Wenckebach), Mobitz II second degree AV block and third degree AV block (complete heart block).

First degree AV block, defined as PR interval >0.20 seconds, is common in athletes and other fit people such as aircrew. If the airman is asymptomatic without evidence of structural heart disease, there should be no limitations for flying or flying training.<sup>1</sup> Second degree AV block is separated into Mobitz types I and II. In type I block (Wenckebach) there is progressive delay between atrial and ventricular contraction (PR interval) with an eventual dropped beat. In most cases, Mobitz type I block does not produce any symptoms and further evaluation is normally not indicated.<sup>2</sup> Like first degree AV block, second degree Mobitz type I AV block is at or above the AV node and thus likely secondary to increased Vagal tone which is common in healthy airmen. Mobitz I second degree AV block is thus considered a normal variant and requires no further evaluation. Both first degree AV block and second degree Mobitz type I AV block can

be intermittent and occur more often during sleep so are commonly found on Holter monitoring during sleep rather than on a 12-lead ECG performed while awake. In Second degree Mobitz type II block, as with type I block, there is a dropped beat; however, in type II block the PR interval is unchanged prior to and after the dropped beat. The site of involvement for type II block is often below the AV node which puts the patient at a considerable risk for progression to complete heart block (third degree heart block). In third degree AV block (complete heart block), there is complete AV dissociation and the atrial and ventricular rates are independent of each other.

First degree AV block and Mobitz I AV block have been reported on ECG in 0.6% and 0.004% of aviators, respectively.<sup>4</sup> In this population these two findings are usually normal variants related to increased baseline vagal tone, especially in physically active individuals. Presentations due to underlying heart disease would be very unusual in our population, but should be considered in appropriate clinical scenarios. The site of the conduction delay is most commonly in the AV node. Exercise reduces vagal tone and typically reverses these two blocks. First degree AV block previously required a "hopogram" (exercise in place to increase heart rate) for evaluation. In 1999, the USAF Central ECG Library reviewed its database of 72 hopograms done for first-degree AV block. No cases of AV conduction system disease were found. Consequently, hopogram is no longer routinely required and first degree AV block is considered to be a normal variant.

Mobitz II second-degree AV block and third degree AV block have been reported on ECG in 0.003% and 0.004% of aviators, respectively. They generally are recommended for permanent pacemaker placement due to their **potentially sudden** bradycardia-related **hemodynamic impairment with syncope/presyncope**.<sup>4</sup> They are not compatible with continued flying status and are also disqualifying for retention in the military.

#### IV. Aeromedical Concerns.

Aeromedical evaluation is usually not indicated for first degree AV block and Mobitz I AV block, but the USAF Central ECG Library/ACS may request further local evaluation for unusual individual cases, such as first degree AV block with marked PR prolongation (usually >0.30 seconds), first appearance of either of these two blocks at an older age (usually >40 years), or frequent Mobitz I on an ECG or other tracing, especially while awake. Both Mobitz II second degree AV block and third degree AV block are at risk for sudden death, syncope, bradycardia-related hemodynamic symptoms and heart failure.

| ICD 9 Codes for AV conduction disturbances |   |  |
|--|---|--|
| 426.0                                      | Atrioventricular block, complete                    |  |
| 426.11                                     | First degree atrioventricular block                 |  |
| 426.12                                     | Mobitz (type) II atrioventricular block             |  |
| 426.13                                     | Mobitz (type) I [Wenckebach] atrioventricular block |  |

| ICD-10 Codes for AV conduction disturbances |   |
|---|---|
| I44.2                                       | Atrioventricular block, complete        |
| I44.0                                       | First degree atrioventricular block     |
| I44.1                                       | Mobitz (type) II atrioventricular block |
| I44.39                                      | Other atrioventricular block vs. I44.1  |

# V. References.

- 1. Link MS and Pelliccia A. Electrocardiographic abnormalities and conduction disturbances in athletes. UpToDate. Jan 2014.
- 2. Sauer WH. Second-degree atrioventricular block: Mobitz type I (Wenckebach block). UpToDate. Jul 2014.
- 3. Sauer WH. Second-degree atrioventricular block: Mobitz type II. UpToDate. Jul 2014.
- 4. Rayman RB, Davenport ED, Dominguex-Mompell R, et al. Cardiology. Ch. 2 in *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed. New York: Castle Connolly Graduate Medical Publishing, LTD, 2013.

# Attention-Deficit/Hyperactivity Disorder (ADHD) (Jun 2019)

Reviewed: Lt Col Kevin F. Heacock (ACS Neuropsychiatry Branch Chief), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Restructuring of Waiver Guide, Consistent with MSD, AIMWTS review

### I. Waiver Considerations.

Attention-Deficit/Hyperactivity Disorder (ADHD) is disqualifying for all flying duties in the US Air Force. A waiver may be considered for flying if the candidate has established academic and occupational stability off medication for a period of at least 12 months. Any candidate who took medications purely for academic enhancement, without a true diagnosis of ADHD, will still need to show adequate academic or occupational stability off medication for at least 12 months before a waiver is considered. The use of psychostimulants solely to optimize cognitive performance is strictly prohibited (Medical Standard Directory (MSD), Section Q, Note 4). Such unauthorized performance enhancement may be an indication of impaired performance and may prompt unfavorable administrative consequences.

A waiver is NOT required for candidates with a prior diagnosis of ADHD if they have not used medication and have not received special accommodations for occupational or academic performance in the last 4 years (MSD, Q8).

Currently, no stimulant medication is aeromedically approved. Although bupropion is aeromedically approved for smoking cessation and other mental health diagnoses, its use in treating ADHD in the aviation community is unauthorized. To date, no waiver has been granted for ADHD controlled on medication.

Table 1: Waiver potential for ADHD

| Tuble 1: Walver potential for ADID |   |                       |
|------------------------------------|---|-----------------------|
| Flying Class (FC)                  | Waiver Potential                          | ACS Review/Evaluation |
|                                    | Waiver Authority                          |                       |
| I/IA                               | Maybe <sup>1</sup>                        | Yes <sup>2</sup>      |
|                                    | AETC                                      |                       |
| II/III                             | Maybe <sup>1</sup><br>MAJCOM <sup>4</sup> | Yes <sup>2</sup>      |
| RPA Pilot                          | MAJCOM <sup>4</sup>                       |                       |
| GBO/ATC                            | Maybe <sup>1</sup>                        | Maybe                 |
| SWA                                | MAJCOM <sup>3</sup>                       | -                     |

<sup>1</sup> Individuals with adequate school and/or work performance with no medication use or special accommodation for 4 years do NOT require a waiver. No waiver has been granted to date for ADHD controlled on medication.

- 2 ACS review/evaluation if requested by AETC for initial FC I/IA, FC II and FC III applicants.
- 3 For untrained FC II and III, ATC, and GBO personnel, waiver authority is AETC; otherwise, it is the MAJCOM

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# A. Initial Waiver Request:

- 1. Obtain and include all school transcripts from grade school and above.
- 2. See Mental Health Waiver Guide Checklist
- 3. If the local base is unable to provide all required items, they should explain why to the waiver authority.

# B. Renewal Waiver Request:

- 1. Obtain and include all school transcripts not submitted with the initial waiver request.
- 2. See Mental Health Waiver Guide Checklist
- 3. If the local base is unable to provide all required items, they should explain why to the waiver authority.

# Please feel free to contact the ACS Neuropsychiatry Branch with questions:

ACS Aerospace Medicine Branch, USAFSAM/FECA c/o Neuropsychiatry Branch 2510 Fifth Street Bldg 840 Wright Patterson AFB, OH 45433-7913

Fax: (937) 904-6296 DSN: 674-9296

# USAFSAM.FE.PsychiatryMailbox@us.af.m

Comm: 937-938-2768

DSN: 798-2768

# **Aerospace Medicine Waiver Guide**



#### III. Aeromedical Concerns.

Symptoms of ADHD are incompatible with flying duty. However, psychiatric diagnoses made during childhood or as adults are occasionally found to be unsubstantiated in light of a careful, accurate history. This is particularly true in adults if the service member has had no symptoms since early childhood. The more subtle learning and cognitive inefficiencies that can degrade performance under the demands of military flying may not be detected or recognized in prior non-flying pursuits. As it is unlikely that an initial flying applicant or rated aviator would self-identify as suffering from ADHD, the clinician must have a high index of suspicion for this disorder. Complaints may come to the attention of the flight surgeon through the reports of spouses, supervisors, colleagues or other aircrew. In such cases, it needs to be stressed that the aviator's behavior must be sufficiently ageinappropriate, excessive, long-term, and pervasive. The flight surgeon or other clinician who suspects ADHD must attempt to establish a retrospective childhood diagnosis. Diagnostic skepticism is warranted in the context of a referral for poor performance when there is no prior history of cognitive or behavioral problems. Since the diagnosis of ADHD is a clinical one, a comprehensive interview plus careful neuropsychological testing are important diagnostic procedures.

A confirmed diagnosis of ADHD is disqualifying for flying duties. In fact, ADHD is disqualifying for accession into the Armed Forces of the United States if school or work accommodations continued after age 14, there was a history of comorbid mental health disorders, medication was prescribed in the previous 24 months, or there was documentation of adverse academic or occupational performance (DoDI 6130.03 March 30, 2018). The Air Force will process accession waivers if the individual demonstrates at least 15 months of performance stability, off medication immediately preceding enlistment or enrollment (Sec AF Memo 9 Jan 2017).

Use of medication to control ADHD remains incompatible with flying. Further, ADHD can put both aviation duties and military retention at risk if treatment with medication is required for adequate duty performance. If unable to perform without medication, or if unable to meet AFSC qualifications due to the need for medication, referral to the unit commander for determination of administrative disposition is appropriate and a 469 Mobility Restriction should be created stating the member will need a waiver for deployment consideration. If treatment with medication is not required for adequate duty performance, the member remains suited for continued military service. A waiver is required for all flying classes with a history of ADHD treated or requiring special accommodations within the last 4 years.

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder, and as such, manifests during the developmental period interfering with the trajectory of normal growth and maturation. The diagnosis of adult ADHD should not be made without a history of symptoms beginning in childhood, usually before the age of twelve. ADHD is

characterized by "impairing levels of inattention, disorganization, and/or hyperactivity-impulsivity."

Until the past couple of decades, little thought was given to adult manifestations of ADHD. Clinicians now realize this disorder, once believed to "burn out" in adolescence, can persist into adulthood. In childhood, boys outnumber girls by as much as 10 to 1, but the disorder seems to persist in a higher proportion of girls, and by adulthood the ratio of men to women approximates 1 to 1.

Longitudinal studies have shown that ADHD symptoms persist into adult life. Research has shown that adults with the diagnosis of ADHD have a threefold increase risk of motor vehicle collisions, and an increase of industrial accidents are seen whether treated with medication or not. A very large prospective study from Denmark demonstrated individuals diagnosed with ADHD had higher mortality than the general population.

Treatment of ADHD in adults is similar to that of children, although the results in adults are much less predictable than in children. The mainstay of treatment in both groups is pharmacologic treatment with stimulants, which have demonstrated a clinically and statistically significant effect on reducing ADHD symptoms, although some trials have shown that 30% to 50% of adult subjects either do not respond or have adverse effects. There has been some recent success with non-stimulant medication, particularly atomoxetine and bupropion. Others believe that the issue with many "non-responding" adults is that they are probably under-dosed. Non-pharmacologic treatment of ADHD in adults has not been studied. However, it is accepted that psychological treatment (often in a group setting) can improve patients' lives by teaching them how to structure their environment and improve their organizational skills, how to improve social skills and relationships, and how to manage mood liability.

AIMWITS search from Jan 2014 through May 2019 revealed 149 cases; with 91 of them resulted in a disqualification disposition. There were a total of 6 FC I/IA cases with 5 were disqualifications, 28 FC II cases with 14 disqualifications, 11 RPA pilot cases with 5 disqualifications, 83 FC III cases with 53 disqualifications, 18 ATC/GBC cases with 11 disqualifications, and 3 MOD cases with 3 disqualifications.

| ICD-9 codes for ADHD |  |  |
|----------------------|--|--|
| 314.00               | ADHD, predominantly inattentive presentation           |  |
| 314.01               | ADHD, predominantly hyperactive/impulsive presentation |  |
| 314.01               | ADHD, combined presentation                            |  |
| 314.01               | ADHD, unspecified                                      |  |

| ICD-10 codes for ADHD |  |
|-----------------------|--|
| F90.0                 | ADHD, predominantly inattentive presentation           |
| F90.1                 | ADHD, predominantly hyperactive/impulsive presentation |
| F90.2                 | ADHD, combined presentation                            |
| F90.9                 | ADHD, unspecified                                      |

# V. Suggested Readings

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- 4. Dalsgaard S, Østergaard SD, Leckman JF, et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. Lancet, 2015; 385(9983): 2190-96
- 5. Medical Letter. Drugs for ADHD. Vol. 57 (Issue 1464), Mar 2015.
- 6. Adler LA, Spencer JT, Stein MA, and Newcorn JH. Best Practices in Adult ADHD: Neurobiology, Pharmacology, and Emerging Treatments. Expert Roundtable Supplement to CNS Spectr, 13:9 (Supp 13), September 2008.

# Back Pain (Chronic Low) (Feb 2019)

Reviewed: Major Joshua Shields (RAM 20), Dr. Dan Van Syoc (ACS Division Deputy Chief), Col Brandon Horne (AF/SG consultant for orthopedics), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New format

#### I. Waiver Consideration

Recurrent disabling back pain or back pain requiring external support is specifically disqualifying for Flying Classes I/IA, II, III and SWA. ATC/GBO personnel are would be disqualified based on this definition: "Chronic back or neck pain, regardless of cause, which requires ongoing duty or deployment restrictions for over a year, or ongoing specialist follow-up more than annually, or frequent duty absences, or chronic/recurrent use of controlled medications, schedule II-IV."

Table 1: Waiver potential for chronic low back pain

| Flying Class (FC) | Condition                 | Waiver Potential | ACS Review/ |
|-------------------|---------------------------|------------------|-------------|
|                   |                           | Waiver Authority | Evaluation  |
| I/IA              | Chronic Pain <sup>2</sup> | No               | No, No      |
|                   |                           | AETC             |             |
| II/III            | Chronic Pain <sup>2</sup> | Yes <sup>1</sup> | No, No      |
| ATC/GBO/SWA       |                           | MAJCOM           |             |

<sup>1.</sup> Waiver is unlikely for untrained personnel.

# II. Information Required for Waiver Submittal

The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for <u>initial waiver</u> for chronic LBP should include the following:

- 1 History Must define the back pain symptomatology; location, radiation, duration, conditions that improve or aggravate the pain, limitations of activities, treatment, and medications. Discuss any "Red Flags" such as bowel and bladder dysfunction and address pertinent negatives.
- 2 Physical exam range of motion, muscle strength, gait, sensation, reflexes, etc.
- 3 Reports of any radiological or neurological studies and lab work to exclude specific causes of back pain.
- 4 All specialty consults/opinions obtained.

<sup>2.</sup> If member does not meet retention standards (Chronic back or neck pain, regardless of cause, which requires ongoing duty or deployment restrictions for over a year, or ongoing specialist follow-up more than annually, or frequent duty absences, or chronic/recurrent use of controlled medications), the waiver authority is AFMRA.

- 5 MEB results if appropriate.
- 6 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

The aeromedical summary for <u>waiver renewal</u> for chronic LBP should include the following:

- Brief history of back pain symptomatology; location, radiation, duration, conditions that improve or aggravate the pain, work-up and treatment. Include the interval history since last waiver with special attention to changes in symptoms, exasperation and work impact.
- 2 All specialty consults/opinions obtained.
- 3 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Chronic LBP refers to spinal and paraspinal symptoms in the lumbosacral region for >12 weeks. Subacute LBP lasts from 4-12 weeks and acute LBP resolves within 4 weeks. The final aeromedical disposition for mechanical LBP due to lumbar strain/sprain and degenerative processes is dependent on the degree of functional residual impairment that remains once treatment and rehabilitation are completed. The flight surgeon must ascertain that the airman can safely perform all flight duties. There should be no significant limitation of motion, loss of strength, or functional impairment that may compromise safe operation of the aircraft, and/or safe egress. If the patient responds well to therapy and there are few or no recurrences, the airman may be eligible for continuation of flight duties. If the LBP is recurrent and disabling it is disqualifying for all flight classes regardless of the cause. LBP due to other causes such as herniated disc, spondylolisthesis, and spinal fractures has unique aeromedical concerns and is discussed in their respective waiver guides.

AIMWTS search in Feb 2019 revealed 454 individuals with waiver dispositions containing the diagnosis of LBP. Of the total, there were 6 FC I/IA cases (4 disqualifications), 146 FC II cases (29 disqualifications), 249 FC III cases (155 disqualifications), 36 ATC/GBC cases (21 disqualifications), and 17 MOD cases (11 disqualifications).

| ICD-9 code for low back pain |         |
|------------------------------|---------|
| 724.2                        | Lumbago |
| 724.5 Backache, unspecified  |         |

| ICD-10 code for low back pain |  |  |
|-------------------------------|--|--|
| M54.40                        | Lumbago with sciatica, unspecified side; M54.41 right side, M54.42 left side |  |
| M54.89                        | Other dorsalgia  |  |

# IV. Suggested Readings

- 1. Wheeler, S., Evaluation of Low Back Pain in adults. UpToDate Sept 2018
- 2. Knight, Christopher. Treatment of acute low back pain. UpToDate. Sept 2018.
- 3. Chou, R., Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment. UpToDate. Sept 2018.
- 4. Rainville J. Exercise-based therapy for low back pain. UpToDate. Sept 2018.
- 5. Delitto A., Clinical Practice Guidelines for Low Back pain. Orthopt.org. 2012.

# Bell's Palsy (May 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated Table 1 and References

#### I. Waiver Consideration

An isolated episode of Bell's palsy with full recovery and no clinical or functional residua is not aeromedically disqualifying and does not require waiver. An isolated episode of Bell's palsy with incomplete clinical recovery or recurrent episodes of Bell's palsy is disqualifying for all flying classes, and the flyer will be considered for a waiver based on the outcome of treatment and level of post-treatment residual defects. A history of remote Bell's palsy will not necessarily be disqualifying as there is often complete resolution and affected individuals are not at an increased risk of recurrence.

Table 1: Waiver potential for Bell's Palsy

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------|------------------|--------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | Yes                      |
| FC II/III/SWA     | Yes <sup>1</sup> | MAJCOM           | Yes                      |
| ATC/GBO           | Yes <sup>1</sup> | MAJCOM           | No                       |

<sup>1.</sup> Waiver consideration based on amount of residual symptoms and deficits.

Indefinite waiver recommendation possible with complete resolution or minimal residua.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

# A. Initial Waiver Request:

- 1. Complete history of event detailing all symptoms, treatment (all medications, dosages, and number of days treated) and level of symptom resolution.
- 2. Copies of relevant clinical notes, diagnostic studies, imaging reports and images, and operative reports (if applicable). If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical and neurologic examinations.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2. Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical and neurologic examination findings.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual symptoms on operational safety and mission effectiveness, and future risk of symptom recurrence. Aviators with Bell's palsy may have eye irritation due to the inability to close the lid, and food and saliva can pool on the affected side of the mouth potentially spilling out from the corner. Vision can be adversely affected due to the dry eyes, speech may be difficult due to facial weakness, and the wear of life support gear, particularly a tight-fitting aviator mask, can be compromised due to facial weakness. These symptoms make flying inadvisable until resolution of the condition. As most cases will be treated with steroids and possibly antiviral agents, the aviator should be grounded during treatment as these medications are not aeromedically-approved and are unlikely to be recommended for waiver.

AIMWTS review in Feb 2019 revealed 42 cases with the diagnosis of Bell's Palsy. Breakdown of the cases revealed: 3 FCI cases, 13 FC II cases, 1 RPA pilot case, 23 FC III cases, and 1 GBC case. There were 4 disqualifications, all FC III. Two of the DQ cases were for a significant nerve deficit and the other 2 for other diagnoses. Two pilots demonstrated very mild facial weakness, one FC I applicant showed a mild hemifacial spasm, a flight surgeon had residual lagophthalmos, and one pilot showed mild facial asymmetry.

| ICD 9 codes for Bell's Palsy |                                    |  |
|------------------------------|------------------------------------|--|
| 351                          | Facial nerve disorders             |  |
| 351.0                        | Bell's palsy                       |  |
| 351.9                        | Facial nerve disorder, unspecified |  |

| ICD-10 codes for Bell's Palsy |                                    |  |
|-------------------------------|------------------------------------|--|
| G51.8                         | Facial nerve disorders             |  |
| G51.0                         | Bell's palsy                       |  |
| G51.9                         | Facial nerve disorder, unspecified |  |

# IV. Suggested Readings

- 1. Reich SG. Bell's palsy. Continuum (Minneap Minn) 2017; 23(2):447-466
- 2. Ronthal M. Bell's palsy: treatment and prognosis in adults. UpToDate, Nov 5, 2019.

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#### WAIVER GUIDE

Updated: May 2014

Supersedes Waiver Guide of Nov 2010

By: CDR Michael Acromite (ACS RAM and OB/GYN), and Dr Dan Van Syoc

# **CONDITION:**

**Birth Control (May 2014)** 

#### I. Waiver Consideration.

A waiver is not required for hormonal contraception using <u>approved</u> medications that are well tolerated without significant adverse effects. A waiver is not required for LARC methods appropriately placed and well tolerated. A waiver is not required for a history of successful sterilization surgery after a full recovery with appropriate follow-up, and without chronic adverse effects.

# II. Information Required for Waiver Submission.

N/A

#### III. Overview.

Air Force aviators' lives are fully occupied with training, qualifications, deployments, and sorties. As such, family planning can create some challenges. Aviators desiring to conceive generally attempt to plan for this event around mission, career, and family. This may involve deferring conception until the time, location, and circumstances provide a safe opportunity. Pregnancy, especially when unplanned, can create a variety of considerations for the operational and aviation environments. An unplanned pregnancy prior to or during a deployment can create unexpected risks to an individual and mission, while appropriate knowledge, prevention, and planning can significantly reduce the associated operational risks. Estimates for the general population show that half of all pregnancies are unplanned and in approximately half of these unintended pregnancies, contraception of some type was being used.<sup>1,2</sup> Safe and effective contraception that has been appropriately selected and used can play an important preventive role, and flight surgeons can assist in this regard. A variety of effective contraceptive options are currently available to men and women. Factors to consider when a couple is choosing a contraceptive method include its safety, efficacy, convenience, duration of action, reversibility (once the decision to conceive has been made), effect on uterine bleeding, frequency of adverse side effects, affordability, protection against sexually transmitted diseases, and a wish for a more permanent solution. Underlying conditions or risk factors must be considered in women using or planning to use a birth control method.

BENEFITS: While the currently available methods provide short-term or long-term, and reversible or permanent contraception, many gynecological or other medical conditions can be treated with the hormonal contraceptives. Hormonal contraception can provide operational benefit. Physical or emotional stress can produce physiological responses

which have reactionary effects on the pituitary-ovarian hormonal axis. This can result in irregular menstrual cycles, irregular bleeding, menorrhagia, or amenorrhea during the periods of stress. Hormonal contraceptives can sustain hormonal levels that maintain regular menstrual cycles or amenorrhea in the face of these stress effects. In addition, hormonal contraception can be used to treat gynecological conditions such as abnormal uterine bleeding, endometriosis, dysmenorrhea, polycystic ovaries, uterine fibroids, and endometrial hyperplasia.<sup>3</sup> OC are commonly used as the first-line treatment for endometriosis.<sup>4</sup> They also can be used to treat non-gynecological conditions such as acne, hirsutism, menorrhagia-related anemia, premenstrual disorders, and some headaches (not migraine with aura). Oral contraceptives (OC), particularly those containing desogestrel may provide a benefit for menstrual migraine headaches (without aura). OC containing desogestrel, norgestimate, or drospirinone can benefit acne. Drospirinone containing OC are FDA approved for treatment of acne and premenstrual dysphoric disorder. Oral formulations are preferred for treating acne, hirsutism, or androgenic effects due to their first-pass effect which increases hepatic sex-hormone binding globulin, which preferentially binds free androgens. OC may have effects on lipids and should be considered in those with hyperlipidemia. OC containing first generation progestins have a more beneficial effect than second or third generation progestins.

CANCER RISK-BENEFITS: Hormonal contraceptives can reduce risk of some cancers. Up to a 50% reduction in endometrial cancer has been associated with hormonal contraceptive use, particularly with higher potency progestins.<sup>5</sup> The progesterone secreting IUD has also been used to suppress the endometrium and treat endometrial hyperplasia. A reduction in ovarian cancer risk has been associated with hormonal contraceptive use for as little as six months. A 27% reduction in ovarian cancer has been associated with hormonal contraceptive use with benefits of up to 20% in five years of use.<sup>6</sup> An 18% drop in colorectal cancer has been associated with their recent use, while this effect with longer use is uncertain.<sup>7</sup>

ADVERSE EFFECTS: Some contraceptive choices may be associated with increased risks when used in the presence of certain underlying conditions. Estrogen containing hormonal contraceptive can increase the risk of thrombosis in any woman, especially those who are over age 35 and smoke, those with thrombophilia, or those with migraine with aura. A headache history of *migraine with aura is a contraindication* for estrogen containing oral contraceptives due to a significant increase risk of stroke. Some hormonal contraceptives such as DMPA may exacerbate depression in some cases. Progesterone-only methods may decrease bone mineral density in some women with long-term use and should be considered.<sup>8,9</sup> Other potential adverse effects observed include weight gain, nausea, or vomiting. Alternative formulations with a different progestin may address these potential effects. In general, the benefit of each contraceptive method must be weighed against potential or observed adverse effects.

OPTIONS FOR WOMEN: Contraceptive options for women include abstinence, natural methods, barrier methods, oral contraceptive pills, hormonal injections, transdermal patches, vaginal rings, intrauterine devices, sub-cutaneous devices, and permanent sterilization. Natural methods refer to the timing of intercourse that does not involve the

days surrounding an expected ovulation. To be successful, natural methods require predictable cycles, assessment of basal body temperature and cervical mucus, knowledge of effective application, and a highly motivated and disciplined couple. Barrier methods for women include the diaphragm and female condom. The barrier methods also require diligence and are most effective when used in conjunction with a spermicidal lubricant. If used properly, the failure rate can be as low as 2.4 per 100 woman-years.<sup>10</sup>

ORAL CONTRACEPTIVES: In the US, the combined estrogen-progestin oral contraceptive (OC) preparations are the most commonly used effective and reversible method of contraception, with pregnancy rates reported as less than 0.5 per 100 womanyears. While OC use is common and effective, it has a higher discontinue rate within the first year than long-acting reversible devices. Most OC compounds include 35 µg or less of estrogen along with varying types and amounts of progestins. The various progestins include first, second, or third generation forms, with differing profiles relating to their estrogenic effects, progesterone effect, and androgenic effect. Progesterone activity is highest, and estrogenic activity is lowest in the second and third generation progestins. Androgenic activity is highest in the second generation and lowest in the third generation progestins. The progestin, drospirinone has spironolactone-like activity and may help with bloating, but may cause increased potassium levels. The progestins vary in their beneficial and adverse side effects regarding breakthrough bleeding, acne, bloating, headaches, lipid profiles, and premenstrual mood symptoms. Modifying OC use with these in mind may improve benefits, reduce adverse effect, and improve compliance.

STARTING, CHANGING, USING, AND STOPPING: OCs can be started anytime during the menstrual cycle. Traditionally, OC usage has begun on the first Sunday after menses begins, but may be started on the day the prescription is given provided that pregnancy has been excluded. It is important that the woman take the pill every day, because missed pills are the most common cause of contraceptive failure. 1, 10 Progesterone-only oral contraceptives must be taken every day, but also need to be taken at the same time each day to be most effective. The progesterone dominant effect of combination OC generally results in endometrial suppression with shorter and lighter menstrual flow. These combination OC may be taken with or without a placebo (withdrawal) week. Cyclic dosing includes a placebo (withdrawal) week, which usually produces a small menses. Continuous dosing avoids a placebo (withdrawal) week for three or more cycle months. This continuous method generally results in consistent amenorrhea until subsequent withdrawal. Continuous dosing can be used for specific conditions requiring menstrual suppression or used for user preference. When first starting an OC or starting a new formulation OC, it is not uncommon to have irregular spotting for the first few cycles and up to five months for some women. As the woman's body adjusts to the new OC, the menses become lighter and predictable in the monthly cycle, and some experience amenorrhea. Because of this adjustment period, it is generally recommended to continue a new OC trial for five months before considering stopping or changing for minor adverse tolerance effects. More severe adverse effects may require an earlier OC stop or change, but the adjustment period must still be considered subsequently. Resumption of ovulation may occur as soon as a single missed day of an OC, so caution must be advised. After stopping, there may be a variable delay in the

return of normal menstrual flow, ovulation, and fertility, which may be up to six months for OC and up to one year for depot medroxyprogesterone acetate (DMPA).

PROGESTERONE-ONLY: Progesterone-only hormonal birth control is an option for women who desire to use hormonal birth control, but have conditions for which they must avoid estrogen. Progesterone-only methods include the norethindrone pill (Micronor®, Nor-QD®), the etonogestrel single-rod implant (Implanon®), and injectable depot medroxyprogesterone acetate (Depo-Provera®). The progesterone-only pills must be taken at the same time every day, are associated with more unscheduled (breakthrough) bleeding and slightly higher failure rates than traditional OCs. The etonogestrel subcutaneous implants must be placed by a provider trained in the technique according to the manufacturer. DMPA is the only injectable contraceptive option in the US. In most cases, it is given by deep intramuscular injection (150 mg) and is effective for three months. A lower-dose (104 mg) DPMA formulation (Depo-subQ Provera®), is administered subcutaneously every three months. Etonogestrel sub-cutaneous implants and DMPA have been proven effective for control of endometriosis and menstrual conditions, but have been associated with decreased bone mineral density (BMD) with prolonged use.<sup>8,9</sup> While BMD may be decreased in some women, these methods are still considered for their effective contraceptive, symptomatic, and medical benefits with appropriate monitoring and supplementation. The progesterone-only methods typically result in amenorrhea following initial cycles of irregular menstrual bleeding, but some women discontinue their use for persistent irregular spotting.

LARC: Another category of contraception includes the long acting reversible contraceptive (LARC) methods. The LARC methods continue to increase in use with reportedly lower pregnancy rates and higher continuation rates than OC.<sup>11</sup> The three currently available LARC methods include one contraceptive implant and two intrauterine device (IUD) types. The FDA approved contraceptive implant is the etonogestrel single rod contraceptive implant (Implanon®). This single rod implant secretes the progestin, etonogestrel systemically to suppress ovulation and the endometrium for contraception. This implant may remain in place for three years. It requires provider to complete manufacturer training before beginning to insert them in patients. The two FDA approved IUDs include the copper T380A IUD ("Copper T") and the levonorgestrel intrauterine system (Mirena®). The Copper T is a non-hormonal, T-shaped device that is immediately effective on insertion, and may remain inserted for 10 years. The levonorgestrel intrauterine system is a T-shaped device that secretes a small daily dose of the progestin, levonorgestrel that provides a hormonal suppressive effect on the endometrium with little systemic absorption. This IUD can remain in place up to five years. These IUDs are approved for use in nulliparous patients, and are not associated with an increased risk of pelvic inflammatory disease, ectopic pregnancy, or post-use infertility. 11, 12 IUDs are often associated with an increased menstrual discomfort during the first menses following insertion, but typically resolves spontaneously by subsequent months. Non-steroidal antiinflammatory medications provide sufficient relief if this is encountered in the first menses. All the LARC methods are effective contraception, require little ongoing effort to retain contraception, and allow a prompt return of fertility upon removal.

PATCH AND RING: Additional options available to women are the transdermal patch (Ortho Evra®) and vaginal ring (NuvaRing®). They act similarly to OC, but are not taken orally and as such require a lower dose by avoiding a "first pass" hepatic effect. The patch is applied once weekly for three weeks followed by one week without application. The efficacy of the patch has been found to be similar to OC with a high user satisfaction. The contraceptive vaginal ring is a flexible ring inserted into the vagina that releases estrogen and progestin at a constant rate for the three-week period of use. The ring has been found to have an effectiveness rate similar to OC, a low incidence of adverse events, and a high satisfaction rate among users. Both of these methods have the additional benefit of easy reversibility after cessation of use.<sup>2</sup>

PERMANENT METHODS: Some women desire permanent sterilization. These surgical procedures include tubal ligation, or tubal obstruction. Some of these methods are potentially reversible, but the patient needs to be counseled that these procedures are intended to be permanent. Surgical procedures in the operating room include laparotomy, mini-laparotomy, or laparoscopy to excise or cauterize portions of each tube, or place sutures, bands, or clips to obstruct tubes. A convenient time to perform at tubal ligation/obstruction procedure is in the postpartum period. Women under age 26 and those having the procedure in the postpartum period, are most likely to regret sterilization. A more recent method is the "no-incision tubal ligation" (Essure ®) in which obstructing metal coils are placed into the proximal tube from inside the uterine cavity during hysteroscopy. Close follow up with the obstetrician is necessary following the insertion and requires a radiological dye confirmation after three months. This method is permanent and provides no possibility of reversal. Pregnancy after tubal sterilization is uncommon, but has an increased risk of ectopic pregnancy when pregnancy does occur.<sup>1</sup>

OPTIONS FOR MEN: For men, two effective methods include condoms and vasectomy. Condoms are convenient in that they are readily available and do not require a prescription. Correct condom use requires use with each intercourse event, not removed until after intercourse is completed, and used with a spermicidal agent. When used correctly, their effectiveness can approach that of hormonal contraceptives with an additional benefit of protection against most sexually transmitted diseases. A permanent method for men is vasectomy, which is a permanent sterilization technique. Vasectomy is the most commonly performed urologic surgical procedure performed in the US, with an estimated 500,000 each year. Vasectomy is less expensive and associated with less morbidity and mortality than female tubal procedures. It is employed by nearly 11% of all married couples, but is less prevalent than is tubal procedures in women. As with tubal surgical procedures for women, adequate counseling is necessary to discuss that the procedure is designed to be permanent and failures can rarely occur. With an experienced surgeon and a post vasectomy semen analysis performed to confirm effectiveness, it is unusual to have a pregnancy result months to years after the procedure. 

13, 14

# IV. Aeromedical Concerns.

The contraceptive and medical benefits of hormonal and non-hormonal contraceptives are well established. Certain risks should be considered related to aviation. Distracting

symptoms are most common when starting an OC, other hormonal contraception, or LARC. This should be considered after their initiation and monitored for significant symptoms or adverse effects during this time. Users should be encouraged to report adverse effects. IUD may be associated with increased menstrual pain, especially during the first cycle. Irregular spotting or other transient symptoms are more common in the first 1-5 months of a hormonal contraceptive use. Estrogen containing OC may be associated with hypertension, headache, nausea, or vomiting. Persistent hypertension is a reason to discontinue a hormonal contraceptive method to consider an alternative. Underlying conditions must be considered in women using or planning to use hormonal contraceptive methods. Estrogen containing OC are not recommended for women with uncontrolled hypertension, or diabetes with end-organ damage. Estrogen containing OC are associated with an increased risk of venous thromboembolism (VTE), especially in some women. Women who are over age 35 and smoke are at increased risk of VTE which can be exacerbated with the use of estrogen containing OC. For this reason, estrogen containing OC are not recommended in these women. OC may be beneficial for women with some types of headache, including menstrual migraine, but these estrogen containing OC are contraindicated in women with a history of migraine with aura due to a significant increased risk of stroke. OC with the progestin, drospirinone (Yaz®, Yasmin®) can induce hyperkalemia, in some women through this progestin's spironolactone-like activity, which can also induce diuretic and anti-androgenic effects. If the woman is well screened and has no adverse effects, there is no aeromedical contraindication for the use of oral contraceptives.<sup>15</sup> Female or male surgical procedures for permanent sterilization have uncommon complications or adverse effects. When a sterilization procedure is uncomplicated and results in a full recovery, then there is no restriction to returning to flight status. If a pregnancy is detected in a woman with an IUD in place or a history of a permanent surgical sterilization procedure, an investigation for ectopic pregnancy must be promptly accomplished.

#### V. References.

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#### WAIVER GUIDE

Updated: Jun 2017

Supersedes Waiver Guide of May 2013

By: Lt Col. Paul R. Newbold (RAM 18) and Dr. Dan Van Syoc Reviewed by Col Timothy Phillips, AF/SG consultant for urology

### **CONDITION:**

Bladder Cancer (Jun 2017)

#### I. Waiver Considerations.

History of bladder cancer is disqualifying for all flying classes, as well as for ATC, GBO, and SWA duties. It is also disqualifying for retention, so an MEB is necessary prior to waiver consideration.

Table 1: Waiver potential of bladder cancer.

| Flying Class | Condition           | Waiver Potential | ACS review/evaluation |
|--------------|---------------------|------------------|-----------------------|
| (FC)         |                     | Waiver Authority |                       |
| I/IA         | Stages 0 and I      | Yes#†            | Yes%                  |
|              |                     | AETC             |                       |
| II/III       | Stages 0, I, II and | Yes+*†           | Yes%                  |
|              | possibly early III  | AFMRA            |                       |
| ATC, GBO     | Stages 0, I, II and | Yes+*†           | No                    |
| SWA          | possibly early III  | AFMRA            |                       |

<sup>#</sup> For FC I/IA candidates, waiver may be considered after 5 years of remission, asymptomatic.

Review of AIMWTS database in Jun 2017 revealed 30 waiver submissions for the diagnosis of bladder cancer. There were 4 disqualifications. Breakdown of the cases is as follows: 0 FC I/IA cases, 17 FC II cases (1 disqualified), 2 RPA cases, 10 FC III cases (3 disqualified), and 1 MOD case. The one disqualified FC II case was for high grade disease; two of the FC III disqualified cases were for another medical reason, and the last disqualified case was for a FC III applicant with ongoing therapy and for high myopia.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. Waiver can be considered once the aviator is asymptomatic from both the disease and therapy.

<sup>+</sup> For trained personnel, waiver may be considered six months after treatment completed, in remission and asymptomatic.

<sup>\*</sup> For untrained personnel, waiver may be considered after 5 years of remission.

<sup>†</sup> No indefinite waivers.

<sup>%</sup> ACS review needed only if waiver authority considering a waiver

The AMS for initial waiver for bladder cancer should include:

- A. History symptoms, pathology, stage, treatment, including date of last treatment, surveillance plan and activity level.
- B. List and fully discuss all clinical diagnoses and diagnoses requiring a waiver.
- C. Reports from all imaging studies.
- D. All cystoscopy/surgical reports along with pathology-confirmed histological diagnosis.
- E. Current urinalysis.
- F. Urology/oncology consults to include the quarterly tumor surveillance follow-up in accordance with National Comprehensive Cancer Network (NCCN) guidelines.
- G. Tumor board report, military or civilian, if applicable.
- H. Medical evaluation board results.
- I. Confirmation the aviator does not require continued therapy (other than routine follow-up) and that he or she is free of physical limitations.

The AMS for waiver renewal for bladder cancer should include the following:

- A. History brief summary of stage, treatment, frequency of surveillance and results, any symptoms, activity level; all must be consistent with NCCN guidelines.
- B. Physical pertinent to present case.
- C. Urology/oncology consult.
- D. Labs all urinalysis and cystoscopy results since last waiver.

#### III. Overview.

Bladder cancer is the fourth most common cause of cancer in males and affects men three times more frequently than women. Its incidence also increases with age, with 90% of cases occurring in individuals over age 55. In the U.S., approximately 77,000 new cases and 16,000 deaths occur each year due to bladder cancer. In addition, there are an estimated 500,000 individuals in the US with a history of bladder cancer making its prevalence greater than that of lung cancer. Cigarette smoking is a well-known risk factor, increasing the risk 2-4 fold, and is associated with 50-66% of all bladder cancers in men. Unlike lung cancer, the risk for bladder cancer remains elevated for many years after the smoking cessation, probably accounting for the rising incidence of disease noted in the past few decades. Bladder cancer is much less common in African Americans than in Caucasians, who have the highest rate in the US population.

It has been estimated that occupational exposures may account for up to 20% of all bladder cancer cases. Exposures to toxins in the textile dye and rubber tire industries are risk factors. Historically, these industries used β-naphthylamine, 4-aminobiphenyl and benzidine, all of which were highly associated with bladder cancer. These chemicals have been banned, but the long latency between exposure and disease development makes it difficult to ascertain a definitive relationship for a whole host of other compounds which are still used in these industries. <sup>6</sup> Chronic infection can also be a risk factor for bladder cancer. This is seen more commonly in under-developed countries and thought to be largely related to infection with schistosomiasis. <sup>7</sup>

As with most cancers, prognosis is largely determined by stage and grade; other factors include location of the lesion, number of lesions, and maximum diameter of the largest tumor. The American Joint Committee on Cancer staging system (also known as TNM) is the most widely used system for staging (see Table 2), while the World Health Organization and International Society of Urologic Pathologists published a recommended revised consensus classification system in 2004 (see Table 3). The upper urinary tract should be imaged during initial work up as 5% of bladder cancers can have an associated upper tract lesion.

Urothelial carcinoma, also known as transitional cell carcinoma, is the most common pathologic subtype of bladder cancer and is seen in over 90% of all tumors. Squamous cell tumors account for about 5% of all cases and adenocarcinomas are about 1% of the total. The presenting symptom in the majority of cases is hematuria, which can be either continuous or intermittent. Therefore, the American Urologic Association (AUA) recommended in 2001 that all patients with hematuria, particularly those without evidence of infections, stones or other common causes, undergo cystoscopy and upper tract imaging. The physical exam is unremarkable in most bladder cancer patients, particularly those with non-muscle invasive disease, (which accounts for 70% to 75% of patients). As our aviation population is relatively young, most of the cases will be early in the lifecycle and more likely to be non-muscle invasive in nature.

Table 2: American Joint Committee on Cancer Bladder Staging System<sup>9</sup>

| Stage | Clinical Tumor Stage   |  |
|-------|--|--|
| TX    | Tumor cannot be assessed   |  |
| T0    | No evidence of primary tumor   |  |
| Ta    | Non-invasive papillary carcinoma                                       |  |
| Tis   | Carcinoma in situ: "flat tumor"  |  |
| T1    | Tumor invades subepithelial connective tissue                          |  |
| T2    | Tumor invades muscularis propria                                       |  |
| pT2a  | Tumor invades superficial muscularis propria (inner half)              |  |
| pT2b  | Invades deep muscularis propria (outer half)                           |  |
| T3    | Tumor invades perivesical tissue/fat                                   |  |
| pT3a  | Invades perivesical tissue/fat microscopically                         |  |
| pT3b  | Invades perivesical tissue/fat macroscopically (extravesical mass)     |  |
| T4    | Tumor invades any of the following: prostatic stroma, seminal          |  |
|       | vesicles, uterus, vagina, pelvic wall, abdominal wall                  |  |
| T4a   | Tumor invades prostatic stroma, uterus, vagina                         |  |
| T4b   | Tumor invades pelvic wall, abdominal wall                              |  |
|       | Regional Lymph Nodes (N)   |  |
| NX    | Regional lymph nodes cannot be assessed                                |  |
| N0    | No regional lymph node metastasis                                      |  |
| N1    | Single regional lymph node metastasis in the true pelvis (hypogastric, |  |
|       | obturator, external iliac, or presacral lymph node)                    |  |
| N2    | Multiple regional lymph node metastasis in the true pelvis             |  |
|       | (hypogastric, obturator, external iliac, or presacral lymph node       |  |
|       | metastasis)  |  |
| N3    | Lymph node metastasis to the common iliac lymph nodes                  |  |
|       | Distant Metastasis (M)   |  |
| M0    | No distant metastasis  |  |
| M1    | Distant metastasis   |  |

Table 3 – AJCC Stage Grouping for Bladder Cancer<sup>9</sup>

| Stage | Primary Tumor | Regional Lymph | Distant        |
|-------|---------------|----------------|----------------|
|       | (pT)          | Nodes (N)      | Metastasis (M) |
| 0a    | Ta            | N0             | M0             |
| 0is   | Tis           | N0             | M0             |
| I     | T1            | N0             | M0             |
| II    | T2a           | N0             | M0             |
|       | T2b           | N0             | M0             |
| III   | T3a           | N0             | M0             |
|       | T3b           | N0             | M0             |
|       | T4a           | N0             | M0             |
| IV    | T4b           | N0             | M0             |
|       | Any T         | N1-3           | M0             |
|       | Any T         | Any N          | M1             |

Table 4: WHO Grading Classification of Non-muscle Invasive Urothelial Neoplasia<sup>10</sup>

| Hyperplasia (flat and papillary)                             |
|--|
| Reactive atypia  |
| Atypia of unknown significance                               |
| Urothelial dysplasia   |
| Urothelial carcinoma in situ                                 |
| Urothelial papilloma   |
| Papillary urothelial neoplasm of low malignant potential     |
| Nonmuscle invasive low-grade papillary urothelial carcinoma  |
| Nonmuscle invasive high-grade papillary urothelial carcinoma |

Treatment is largely dependent upon the grade and stage. Therapy can range from transurethral resection of a bladder tumor (TURBT) to radical cystectomy and resection of affected structures. Often, intravesical therapy is used as an adjunct to tumor resection and/or as a prophylactic measure to prevent recurrence.

For non-muscle invasive tumors (defined as stages Ta, Tis, and T1), the initial treatment is a complete TURBT and an examination under anesthesia (EUA) to rule out a palpable mass which would suggest muscle invasive disease. For T1 tumors, up to 30% of cases will be understaged by TURBT, so repeat TURBT is recommended to decrease likelihood of actual understaging. The majority of these non-muscle invasive tumor cases will recur and up to 25% will progress, so rigorous surveillance and follow-up is mandatory. Fluorescence endoscopy after intravesicular instillation of a porphyrin such as hexaminolevulinate may be more effective than white light endoscopic resection for the detection of multifocal tumors, improving the outcomes of TURBT. 12 Intravesical therapy is generally used in the adjuvant setting to prevent further recurrence. Bacillus Calmette-Guérin (BCG) and mitomycin C are widely used as intravesical immunotherapy and chemotherapy agents but others can be used as well. A key point with these agents is that patients often have no side effects for several cycles, and then up to 90% may develop cystitis and up to than 25% will develop fever, malaise, and hematuria.<sup>1,4</sup> These symptoms generally resolve quickly after completion of therapy, which is usually administered once/week for 6 weeks.

For invasive tumors (T2 and above) and for some high grade T1 tumors, radical cystectomy is the recommended therapy, with consideration of neoadjuvant chemotherapy and radiotherapy, depending on stage of disease at presentation and the patient's overall health status. Bladder preservation or sparing treatment using primary chemotherapy and external beam radiotherapy is an option in selected patients with T2 and T3a urothelial carcinomas, but is associated with higher rates of recurrence and disease specific mortality. Often this approach is reserved for patients who are medically unfit for major surgery or for those seeking an alternative treatment course.<sup>5</sup>

Because of a fairly high risk of recurrence for all grades and stages, there will be a lifetime need for disease surveillance. The National Comprehensive Cancer Network provides guidance for surveillance stratified by surgical approach to the primary tumor. Patients treated with cystectomy get laboratory evaluations every three to six months for the first

two years. These tests include urine cytology, liver and renal function tests, and serum electrolytes. Patients treated with cystectomy also get a chest x-ray and abdominal and pelvic CT exams every six to twelve months for the first two years and then as clinically indicated.<sup>5</sup> Patients treated with bladder preservation (TURBT or partial cystectomy) get the same evaluations as patients treated with cystectomy as well as serial cystoscopies with cytological evaluation every three to six months for the first two years, with intervals based on physician discretion.<sup>13</sup> In general, all patients with non-invasive disease can expect a recurrence rate of 50%, but this rate is higher in those with high-grade disease.<sup>3</sup> After two years without recurrence, the recommendation is for indefinite annual exams.<sup>5</sup> Several urothelial malignancy markers have recently been approved by the FDA, but there is currently insufficient evidence for their routine use in detection of new disease or surveillance. 11, 14 One issue with the utilization of markers is the finding of a positive marker with normal cystoscopy. These findings have been termed "anticipatory" positives with some studies suggesting that they detect cancer prior to cystoscopic visualization. Studies are ongoing to determine the incremental benefit of markers and the costeffectiveness of their use. 15

### IV. Aeromedical Concerns.

The aeromedical concerns are based more on the treatment and possible therapy complications than on the disease itself. If the aviator is off all treatment medications and is disease-free (considered to be in remission) and asymptomatic, he or she can be considered for a waiver. Due to a relatively high risk for recurrence, the flyer needs frequent follow up with their urologist. There is low likelihood that recurrence of non-invasive disease would cause sudden incapacitation.

| ICD-9 codes for Bladder Cancer |                               |  |  |
|--------------------------------|-------------------------------|--|--|
| 188                            | Malignant neoplasm of bladder |  |  |
| 233.7                          | Carcinoma in situ of bladder  |  |  |

| ICD-10 codes for Bladder Cancer |  |  |
|---------------------------------|--|--|
| C67.9                           | Malignant neoplasm of bladder, unspecified, C67.x (.08 |  |
|                                 | specific site of bladder)                              |  |
| D09.0                           | Carcinoma in situ of bladder                           |  |

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#### WAIVER GUIDE

Updated: Oct 2017

Supersedes Waiver Guide of Jun 2013

By: Maj Daniel R. Hatcher (RAM 18) and Dr Dan Van Syoc

Reviewed by Lt Col Thomas Stamp, AF/SG consultant in surgery and Lt Col Roger Wood,

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### **CONDITION:**

**Breast Cancer (Oct 2017)** 

#### I. Waiver Considerations

Breast cancer, or a history of breast cancer, is disqualifying for all classes of flying in the United States Air Force, as well as retention. Current policy verbiage states: "Malignant Neoplasms. All malignant neoplasms (i.e. cancer) require I-RILO processing. (Basal cell or squamous cell carcinomas of the skin, and cervical carcinomas-in-situ, after surgical cure are exempt from this requirement if no sequelae.)"

Table 1: Waiver potential of breast cancer

| Flying Class | Condition            | Waiver Potential | ACS review/evaluation   |
|--------------|----------------------|------------------|-------------------------|
| (FC)         |                      | Waiver Authority |                         |
| I/IA         | Stages 0 or I        | Yes#†            | Yes                     |
|              |                      | AETC%            |                         |
|              | Stage IIA, or IIB    | No               | No                      |
|              |                      | AETC             |                         |
|              | Stage III or IV      | No               | No                      |
|              | 2 11.85 55 - 1       | AETC             |                         |
| II/III       | Stages 0, I, IIA or  | Yes+*†           | Yes                     |
|              | IIB                  | AFMRA%           |                         |
|              | Stage III or IV      | No               | No                      |
|              | Stage III of IV      | AFMRA%           | 140                     |
| ATC/GBO      | Stages 0, I, IIA, or | Yes+*†           | At discretion of waiver |
| SWA          | IIB                  | AFMRA%           | authority               |
|              |                      |                  |                         |
|              | Stage III or IV      | No               | No                      |
|              |                      | AFMRA%           |                         |

<sup>#</sup> For Flying Class I/IA candidates, waiver may be considered after five years cancer free.

<sup>†</sup> No indefinite waivers.

<sup>\*</sup> For untrained personnel, waiver may be considered after 5 years of remission.

<sup>+</sup> For trained personnel waiver may be considered as early as six months after treatment completed, in remission, surveillance is ongoing, and asymptomatic.

<sup>%</sup> All waivers need to go to MAJCOM who will then route them to AFMRA after appropriate review at their level. Per AFI 48-123, those medical conditions requiring an MEB need to be waived initially by AFMRA.

AIMWTS review in Oct 2017 revealed a total of 51 individuals with a waiver submission with the diagnosis of breast cancer. Breakdown of the cases revealed: no FC I/IA cases 14 FC II cases (1 disqualified), 28 FC III cases (2 disqualified), no RPA Pilots, 6 ATC/GBC cases (0 disqualified), and 3 MOD cases (1 disqualified). Seven waiver requests were denied. Of the 7 that were denied, 3 were FCII, 3 were FCIII, and 1 was MOD. The highest stage of breast cancer that was successfully waived on several occasions was stage IIb. Of those that were disqualified 3 were for other conditions, 2 were for early submission, and 2 were for advanced stage cancer.

# II. Information Required for Waiver Submission

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. I-RILO must be submitted prior to waiver submission.

The AMS for <u>initial waiver</u> for breast cancer should include the following:

- A. List and fully discuss all clinical diagnoses and diagnoses requiring a waiver.
- B. History- initial symptom or screening used to detect the malignancy. Also include overall health, fitness, family history, prior surgery, and prior illnesses.
- C. Laboratory results: CBC with differential and platelet count, complete metabolic panel including liver function tests, alkaline phosphatase
- D. Current Physical- especially describing any deformity, lymphedema, or restricted range of motion for the upper extremities and chest wall, as well as mental state.
- E. Imaging studies: For stage II or greater, include mammogram, ultrasound, chest X-ray, CT scan of brain and liver, bone scan and or MRI if applicable; PET if applicable.
- F. Pathology findings to include tumor, tumor markers, ER and PR determination, HER2 status, tumor size, location, margins, node status, and means used to obtain lymph nodes.
- G. Surgical operative reports to include placement of any prosthesis, vascular access port, or implant/muscular flap.
- H. Oncology report to include treatment plan and protocol, prognosis, and stage of cancer.
- I. Documentation that the level of follow-up care is consistent with current NCCN standards.
- J. Tumor Board report as applicable.
- K. Medical Evaluation Board report or I-RILO as appropriate.

The AMS for <u>waiver renewal</u> for breast cancer should include the following:

- A. Interim history.
- B. Physical exam of chest wall and axillae regions.
- C. Oncology and Surgery consultation reports.
- D. Laboratory results since last waiver.
- E. Radiological results since last waiver.
- F. Evidence of follow-up care consistent with NCCN standards.

#### III. Overview.

Breast cancer is a malignant proliferation of lobular or ductal epithelium of the breast. The proliferation may be hyperplastic, atypically hyperplastic, in situ carcinoma or invasive carcinoma.<sup>1, 2</sup> Excluding skin cancers, breast cancer is the single most common form of cancer diagnosed in women of all races in the United States. Breast cancer is the number one cause of cancer death in Hispanic women and is the second most common cause of cancer death in Caucasian, African-American, Asian/Pacific Islander, and American Indian/Alaska Native women. In 2013 (the most recent year numbers are available) 230,815 women were diagnosed with breast cancer and 40,860 died from the disease.<sup>3</sup> In 2013 (most recent year numbers available) 2,190 men were diagnosed with breast cancer and 464 died from the disease.<sup>4, 5</sup> The chance of a woman being diagnosed with breast cancer some time during her life is about 1 in 8 and the chance of a woman dying from breast cancer is about 1 in 35. Breast cancer is about 100 times less common among men than among women. Men and women with similar stages of breast cancer have a similar outlook for survival, although men are often diagnosed at a later stage. A person with breast cancer in early stages often has no symptoms (breast pain is usually indicative of benign conditions); and even large tumors may be noted as painless masses. Some signs which may (or may not) occur include: persistent breast thickening, swelling, distortion, skin irritation, nipple discharge or abnormalities such as ulceration or retraction (peau d' orange appearance).<sup>3</sup>

# Immutable Risk Factors<sup>1–3, 6–9</sup>

There are a number of risk factors that are beyond the control of patients.

- Female gender
- Older age with risk significantly increase beyond 40 years old
- Genetic risk factors with the most common being BRCA1 and BRCA2
- Family history in a first degree relative
- A previous personal history of breast cancer
- Race with white women having a higher incidence from age 60-84 and black women with a higher incidence before the age of 45. All other races have a lower incidence.
- History of proliferative benign breast disease with or without atypia.
- Dense breast tissue
- Age of menarche before age 12 or menopause after age 55
- History or high dose radiation to the chest between 10 and 30 years old
- Women who took DES or exposed in utero

# Modifiable Risk Factors<sup>1, 7, 10, 11</sup>

There are additional risk factors that are under the control of women.

- Women who have their first child after age 30 as well as women who give birth to few children
- Not breast feeding
- Recent use of oral contraceptives

- Perimenopausal hormone therapy (This risk diminishes to baseline risk over 5 years after stopping)
- Alcohol consumption
- Tobacco use
- Being overweight or obese increase post-menopausal risk through a variety of mechanisms
- Sedentary life style

Note that caution should be taken when population based data is applied to a single person. Therefore, many *breast cancer risk assessment tools* based on different data sets of risk factors have been developed, which can help calculate who is at high-risk and therefore who would benefit from screening modalities beyond mammograms alone. These models include The Gail model, the Claus model, the BRCAPRO, BODAICEA and Tyrer-Cuzic models.<sup>12</sup>

## Detection

Mammography: Mammogram screening has been shown to decrease mortality for breast cancer (by 30% since 1990) and it is the mainstay method. There are multiple organizations that give recommendations for breast cancer screening in women. The major organizations are the US Preventive Services Task Force (USPSTF), the American College of Obstetricians and Gynecologists (ACOG), the American Cancer Society, the Society of Breast Imaging, and the American College of Radiology. 12-14 In deciding what to recommend to and discuss with patients AFI 44-102 (Medical Care Management), published March 2015 and updated January 2017 notes that, "nationally recognized guidelines, such as those published by the ACOG or USPSTF or other similar authority, shall govern the frequency of periodic screening examinations (4.1.3). Medical Treatment Facilities (MTFs) must offer or purchase screening mammograms for all active duty women and other eligible beneficiaries. The initiation and frequency of mammography shall be guided by discussion between the patient and the primary care provider, as well as by current guidelines and incorporating patient risk factors and personal preference (4.2.1). MTFs must make diagnostic breast imaging available to women at any age who have been identified by their healthcare providers as requiring additional evaluation as indicated by individual risk factors (4.2.2)."<sup>15</sup>

*Clinical breast exams* have been identified as having variable utility and risks by the different recommendation organizations. Providers and patients need to again decide the utility of this screening modality after considering the current guidelines and patient preferences.<sup>13, 14</sup>

### Diagnosis:

Once screening or clinical evaluation determine that there is potential breast cancer a tissue biopsy is needed to determine a diagnosis. The type of biopsy should be guided by a breast surgeon or other breast specialist and include fine needle aspiration, stereotactic core needle biopsy, and open surgical biopsy. This process may also include sentinel node

biopsy. Once a sample is processed by pathology it will be given a grade, hormone receptor status, and other biomarker states that are important to treatment options.<sup>2, 4</sup>

# **Breast Cancer Staging:**

There are two staging systems in breast cancer care. The first is the TNM staging system that takes into consideration primary tumor size (T), extent of spread of cancer to the regional lymph nodes (N), and existence of distant metastasis (M). Additionally the staging of breast cancer based is rated into anatomic stage/prognostic groups. This staging system takes the information of the TNM system and places it in stages 0 through IV as described in Table 1. This prognostic grouping is additionally used in helping to determine the aeromedical risk and risk of recurrence.<sup>2, 4, 6</sup>

Table 2: Anatomic Stage/Prognostic Groups<sup>16</sup>

| Table 2: Anatonne Stage/Frognostic Groups |                 |       |                  |  |
|---|-----------------|-------|------------------|--|
| Stage <sup>0</sup>                        | $\mathbf{T}^0$  | $N^0$ | $\mathbf{M}^{0}$ |  |
| 0   | Tis             | N0    | M0               |  |
| IA  | T1 <sup>a</sup> | N0    | M0               |  |
| IB  | T0              | N1mi  | M0               |  |
|   | T1 <sup>a</sup> | N1mi  | M0               |  |
| IIA                                       | T0              | N1    | M0               |  |
|   | T1 <sup>a</sup> | N1    | M0               |  |
|   | T2              | N0    | M0               |  |
| IIB                                       | T2              | N1    | M0               |  |
|   | T3              | N0    | M0               |  |
| IIIA                                      | T0              | N2    | M0               |  |
|   | T1              | N2    | M0               |  |
|   | T2              | N2    | M0               |  |
|   | T3              | N1    | M0               |  |
|   | T3              | N2    | M0               |  |
| IIIB                                      | T4              | N0    | M0               |  |
|   | T4              | N1    | M0               |  |
|   | T4              | N2    | M0               |  |
| IIIC                                      | Any T           | N3    | M0               |  |
| IV  | Any T           | Any N | M1               |  |

<sup>&</sup>lt;sup>a</sup> T1 includes T1mi

<sup>-</sup>T0 and Tq tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

<sup>-</sup>M0 includes M0(i+)

<sup>-</sup>The designation pM0 is not valid; M0 should be clinical

<sup>-</sup>If a patient presents with M1 prior to neoadjuvant systematic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.

<sup>-</sup>Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastasis, provide that the studies are carried out with 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.

-Post neoadjuvant therapy is designated with "yc" or "yp" prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

The stage of a cancer is almost always the most important factor in choosing among treatment options. The following tests may be needed for staging (and follow-up): chest X-Ray, mammogram, ultrasound, CT scan, MRI (for those who are high-risk or whose breasts cannot be adequately imaged with mammography and ultrasound i.e., due to very dense tissue, positive axillary nodes or possible occult primary tumor originating in the breast or to evaluate the chest wall itself), and PET scan (limited use: not recommended for Stage I, IIA, IIB or T3N1M0 due to high false-negative). These radiographic methods may need to be used in concert.

### **Treatment:**

In order to make the best treatment choice for people with breast cancer, the extent of disease locally and systemically, the disease stage, features of hormone receptor/biomarkers and evidence of metastases to lymph nodes and beyond, must be defined. Treatment then becomes a combination of local and systemic therapy.

Treatment decisions are a joint decision between the patient and the physician team after considering tumor staging and biologic markers or the cancer. Early breast cancer treatments usually involve surgery with adjudicative treatment with any combination or chemotherapy, radiation, hormonal therapy, and targeted therapies. Advanced or metastatic disease is generally treated with systemic therapies which option are chemotherapy, hormonal therapy, or targeted treatment.<sup>2,4</sup>

#### Survival:

Using the 2006-2012 NIH Surveillance, Epidemiology, and End Results (SEER) data the following is a brief overview of breast cancer state distribution and 5-year survival.<sup>17</sup>

```
Percent of cases by stage (2006-2012):
Localized (61%)
Regional (31%)
Distant (6%)
Upstaged (2%)
```

5-year relative survival (2006-2012) by age at diagnosis:

```
Age <45 (88.4%)
Age 45-54 (90.6)
Age 55-64 (90.2%)
Age 65-74 (87%)
Age 75+ (90%)
```

5 year relative survival (2006-2012) by stage at diagnosis:

Localized (98.8%)

Regional (85.2%)

Distant (26.3%)

Upstaged (52.5%)

### **IV. Aeromedical Concerns**

Breast cancer, in the early stages, has almost no risk of sudden incapacitation; and it is only in the later stages, with involvement of distant organ metastases, where such risk occurs. However, the treatment of breast cancer can have local and systemic effects which can result in significant adverse impact in the aerospace environment. For instance, mastectomy can be associated with significant muscle and tissue loss, loss of self-esteem, depression, as well as with lymphedema from axillary node dissection. There can also be loss of upper limb mobility from nerve damage during the surgery, particularly if there is damage to the long thoracic and thoracodorsal nerve distributions. Scar tissue and chronic pain can be the result of surgery and/or radiation therapy. All of these situations can adversely affect strength, endurance, comfort, and mobility in the cockpit environment, and may preclude safe wear of equipment and safe operation of an aerospace vehicle. In addition, the systemic effects of chemotherapy (such as nausea, vomiting, blood clots, hot flashes, arthralgia and myalgia) can also adversely affect strength, endurance, and stamina in the cockpit and the aviation environment; and this is not withstanding the very real risks of neutropenia, as well as anemia, which even in its mildest forms can decrease performance at altitude.

| ICD 9 codes for breast cancer |  |
|-------------------------------|--|
| 174.0-174.9                   | Malignant neoplasm of the female breast            |
| 175.0-175.9                   | Malignant neoplasm of the male breast              |
| 217                           | Benign neoplasm of breast (non-metastasizing tumor |
|                               | arising from breast parenchyma)                    |

| ICD-10 codes for breast cancer |   |
|--------------------------------|---|
| C50.111                        | Malignant neoplasm of the central portion of right female   |
|                                | breast, .112 left, .119 unspecified, *quadrant defined 0.2, |
|                                | 0.3, 0.4, 0.5, 0.6, 0.8, 0.9                                |
| C50.121                        | Malignant neoplasm of the central portion of right male     |
|                                | breast, .122 left, .129 unspecified, *quadrant defined 0.2, |
|                                | 0.3, 0.4, 0.5, 0.6, 0.8, 0.9                                |
| D24.1                          | Benign neoplasm of right breast, .2 left, .9 unspecified    |

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#### **WAIVER GUIDE**

Updated: Jan 2016

Supersedes Waiver Guide of Apr 2012

By: Dr. Dan Van Syoc

### **CONDITION:**

Cancers (Misc.) (Jan 2016)

#### I. Waiver Considerations.

According to the AF Medical Standards Directory, the history, or presence of, a malignant tumor, cyst or cancer of any sort is disqualifying for aviation and special duties, as well as for retention. Childhood malignancy considered cured may be considered for waiver on a case-by-case basis. To be considered for a waiver, the malignancy needs to be considered cured, or in remission, by applicable clinical standards. The individual must be off all chemotherapeutic agents for long enough to allow for all the intended clinical effects and for all unintended effects to have resolved. The individual must also have no identifiable aeromedically significant side effects from any treatment modality. Each such case must be submitted to the ACS for review prior to waiver action. All contributing lifestyle issues must be resolved. Generally, waiver will not be considered within six months of cessation of definitive therapies.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> should include the following, at a minimum:

- A. History of tumor diagnosis, all treatment performed and any side effects from the tumor and/or treatment. Need good time lines.
- B. All imaging reports (actual images may be required in some cases).
- C. Surgical reports, consults and pathology reports.
- D. Clinically relevant labs.
- E. Oncology consultation stating malignancy is considered cured, or in remission, and the recommended follow-up schedule for the patient.
- F. Tumor board results if accomplished.
- G. MEB results.

The aeromedical summary for <u>waiver renewal</u> should include the following:

- A. Detailed interim history since last waiver submittal.
- B. All applicable labs and imaging studies.
- C. Consult from oncologist.

#### III. Overview.

Previously, there were several cancer diagnoses in the waiver guide which have since been removed. The reason for so doing is the paucity of AIMWTS submissions in these categories. Causes for this would include: rarity of the tumor in our aviation population, poor prognosis of the tumor once diagnosed, long duration of chemotherapy and hazards associated with a particular drug regimen, and treatment side effects that are not compatible with aviation duties.

Having said this, there are those folks with many types of cancer who defy the odds and do well after an aggressive approach to their disease. After a thorough evaluation it may be determined that they are fit for waiver consideration.

The following malignancies have a current posted waiver guide:

Bladder

**Breast** 

Cervical

Colorectal

Hodgkin Lymphoma

Leukemia

Malignant Melanoma

Non-Hodgkin Lymphoma

**Pituitary Tumors** 

**Prostate** 

Salivary Gland

Testicular

Thyroid

The following malignancies have been removed from the waiver guide:

Carcinoid

Kidney

Laryngeal

Lung

**Neurological Tumors** 

Oral cancers

Other GI tumors

Ovarian

Plasma cell dyscrasias

Uterine

#### IV. Aeromedical Concerns.

As with all malignancies, there is concern with recurrence and sudden incapacitation. There is also concern with side effects of treatment such as surgery, radiation, and chemotherapy. An aviator returned to flying duties after treatment for a malignancy must be able to endure all the rigors of his or her aviation environment as well as to safely

egress the aircraft in case of an emergency. Depending on the tumor and stage, as well as flyer's aircraft, it may be prudent to have the aviator spin in a centrifuge and/or go through altitude chamber training prior to waiver consideration.

## Cardiomyopathy (Dec 2019)

Reviewed: Lt Col Kevin Alford, (RAM 21), Lt Col Eddie Davenport (ACS Cardiology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

**Significant Changes:** Update to aeromedical concerns. Update to waiver considerations. Addition of Special Warfare to Table 1

#### I. Waiver Consideration

Cardiomyopathy is disqualifying for all classes of flying duties. It is disqualifying for retention purposes, and members with all but the most mild degrees of cardiomyopathy will only be considered for aeromedical waiver after the individual has been released to full unrestricted activity and found fit for continued military duty by a medical evaluation board (MEB). For the purposes of this waiver guide, cardiomyopathy includes any disease of the myocardium, reduction in left ventricular ejection fraction (<50%), or clinical diagnosis of heart failure. Heart failure is classified according to the New York Heart Association (NYHA) classes (class I or greater is disqualifying) and the American Heart Association (AHA) stages (stage B or greater is disqualifying). Heart failure also includes heart failure with preserved ejection fraction (HFpEF) when symptomatic. Waiver submissions should be made only after resolution of any acute episode, stabilization of the medical regimen, and release of the individual back to full unrestricted activities by the treating cardiologist. ACS review is required for initial waivers for cardiomyopathy to confirm the diagnosis. Mild cases of dilated cardiomyopathy (DCM) which resolve over time may be considered for waiver after ACS evaluation. Some secondary cardiomyopathies may be waiver eligible, based on policies for the underlying disorder and the impact of the secondary cardiomyopathy on overall prognosis. Typically, this will involve definitive therapy that results in an aeromedically acceptable outcome, including resolution of the cardiomyopathy. Resolution of tachycardia-induced cardiomyopathy and return of left ventricular and left atrial size and function to normal after successful surgical repair of severe mitral regurgitation are examples.

Table 1: Waiver potential for Cardiomyopathy<sup>3</sup>

| Flying Class (FC)   | Condition                | Waiver Potential | ACS                |
|---------------------|--------------------------|------------------|--------------------|
|                     |                          | Waiver Authority | Review/Evaluation  |
| I/IA                | DCM, HCM, RCM, ARVC/D,   | No               | Yes <sup>2</sup>   |
|                     | secondary cardiomyopathy | AETC             |                    |
| II/III <sup>1</sup> | DCM, HFrEF, HFpEF        | Maybe            | Yes <sup>2</sup>   |
|                     |                          | MAJCOM           |                    |
|                     |                          |                  |                    |
|                     | HCM, ARVC/D, and RCM     | No               | Yes <sup>2</sup>   |
|                     |                          | MAJCOM           |                    |
|                     |                          |                  |                    |
|                     | Secondary cardiomyopathy | Yes              | Yes <sup>2</sup>   |
|                     |                          | MAJCOM           |                    |
| ATC <sup>1</sup>    | DCM, HFrEF, HFpEF        | Maybe            | Maybe <sup>2</sup> |
| GBO <sup>1</sup>    | _                        | MAJCOM           |                    |
| SWA <sup>1</sup>    |                          |                  |                    |
|                     | HCM, ARVC/D, and RCM     | No               | Maybe <sup>2</sup> |
|                     |                          | MAJCOM           |                    |
|                     |                          |                  |                    |
|                     | Secondary cardiomyopathy | Yes              | Maybe <sup>2</sup> |
|                     |                          | MAJCOM           |                    |

DCM – Dilated Cardiomyopathy; HCM – Hypertrophic Cardiomyopathy; RCM – Restrictive Cardiomyopathy; ARVC/D – Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia; HFrEF – Heart Failure with Reduced Ejection Fraction; HFpEF – Heart Failure with Preserved Ejection Fraction.

- 1. Initial training cases should all be treated similar to FC I/IA.
- 2. ACS review or evaluation for initial cases is at the discretion of the waiver authority.
- 3. Per AFI 48-123 6.4.1.3., AFMRA remains waiver authority for all initial waivers for conditions that do not meet retention standards, unless 6.4.1.4.1. applies.

## II. Information Required for Waiver Submittal

Aeromedical disposition and waiver submission should only be submitted after administrative and clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for the <u>initial waiver</u> for cardiomyopathy should include the following:

- 1. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- 2. Cardiology consult
- 3. Electrocardiogram (ECG).
- 4. Chest x-ray report.
- 5. Official report of all local echocardiograms. Also upload digitally or send CD/DVD copy of the images of the most recent echocardiogram to the ACS. (Notes 1 and 2)

- 6. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- 7. Results of medical evaluation board MEB (worldwide duty evaluation for ARC members).
- 8. If the local base is unable to provide all required items, they should explain why to the waiver authority.

The aeromedical summary for waiver renewal for cardiomyopathy should include the following:

- 1. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- 2. Electrocardiogram (ECG).
- 3. Additional local cardiac testing is not routinely required for re-evaluation cases followed at the ACS but may be requested in individual cases. If so, the previous ACS evaluation/review will specify details regarding any requested local testing.
- 4. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac catheterization/angiography, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- 5. If the local base is unable to provide all required items, they should explain why to the waiver authority.

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (member's MAJCOM)

USAFSAM/FECI Facility 20840

2510 Fifth Street

WPAFB, OH 45433-7913

For expediting the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

### **III. Aeromedical Concerns**

Cardiomyopathy is disease of the myocardium and can often result in functional cardiac deficits sufficient to affect aviation safety. Academically, the diagnosis of cardiomyopathy is distinct from the clinical syndrome of heart failure, which can be caused by disorders other than those of the myocardium. However, for the purposes of this waiver guide, cardiomyopathy includes any disease of the myocardium, reduction in left ventricular ejection fraction (<50%), or clinical diagnosis of heart failure. Heart failure is classified according to the NYHA classes (class I or greater is disqualifying) and the AHA stages (stage B or greater is disqualifying). Heart failure also includes heart failure with preserved ejection fraction (HFpEF) when symptomatic. The aeromedical concerns due to cardiomyopathy include the risk of sudden incapacitation, altered physiology secondary to the disease process, and the impact of medical treatment. The

risk in these areas varies based on the cause of the cardiomyopathy, the severity of disease, and the treatments used. Cardiomyopathy can be caused by primary disorders of the myocardium or result secondarily to systemic diseases. When a systemic disease is causative, aeromedical risk may be amplified by extra-cardiac manifestations of the disorder. While the natural history of most cardiomyopathies is to progress to more severe disease, some cardiomyopathies – particularly peripartum cardiomyopathy, tachycardia induced cardiomyopathy, and cardiomyopathy secondary to viral myocarditis – may resolve.

The risk for sudden incapacitation is increased in all members with cardiomyopathy due to an increased risk for ventricular arrhythmias. Certain types of cardiomyopathy result in proportionally higher risk for sudden incapacitation. For instance, individuals with Hypertrophic Cardiomyopathy (HCM) and Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) are at high risk for symptomatic and incapacitating arrhythmias. This hazard alone may exceed historical risk tolerances. All aviators in whom the diagnosis of cardiomyopathy is considered require an evaluation for ischemic heart disease, as those with ischemic cardiomyopathy also are at an increased risk for incapacitating ischemic events that can be modified with appropriate treatment. Importantly, the aviation environment may increase the risk for incapacitation. As an example, exposure to high  $+G_z$ s may potentiate ventricular arrhythmias. [Also, those who are not acclimated to intermittent hypoxia may be at higher risk for cardiovascular complications.]

Alterations of cardiac function associated with cardiomyopathies increase the risk to aeromedical safety. Even if any cardiomyopathy associated heart failure is well compensated, aviators may experience decreased exercise tolerance that impairs execution in high-performance aviation. Furthermore, left ventricular dysfunction can reduce capacity to augment cardiac output during exposure to sustained acceleration increasing the risk for G-induced loss of consciousness. Finally, aviators with cardiomyopathy may more poorly tolerate the hypoxic environment of aviation than do their colleagues with normal cardiac function.

Treatments for cardiomyopathy can also have a deleterious effect on aviation safety. For instance, beta blocker ( $\beta B$ ) therapy is recommended by published guidelines for treatment of those with reduced EF primarily to reduce risk of arrhythmia; beta blockers have also been shown to improve cardiac function in subsets of cardiomyopathy patients. [Of note, angiotensin converting enzyme inhibitors (ACE-i) and angiotensin receptor blockers (ARBs) are also recommended in heart failure with reduced EF.] Regardless of the indication,  $\beta Bs$  reduce tolerance for  $+G_z$  acceleration. Similarly, vasodilators such as nitrites and hydralazine, used for symptom management in heart failure would reduce G-tolerance. Medical devices are increasingly used in the management of cardiomyopathy. Those with sufficient cardiac dysfunction or risk of sudden cardiac death to warrant placement of an implantable cardioverter defibrillator (ICD), use of resynchronization therapy, or placement of more advanced devices such as left ventricular assist devices, are not suitable for military aviation.

In the USAF aviator and special operator populations, presumed diagnoses of cardiomyopathy are often identified after routine testing of an asymptomatic individual, such as with a screening EKG. However, young, athletic individuals can develop changes on cardiac testing that may appear similar to those identified in mild cardiomyopathies. For instance, EKG testing in athletic individuals may demonstrate first degree AV block, incomplete right bundle branch block, early repolarization, or QRS voltage criteria for left ventricular hypertrophy in the absence of true pathology. Similarly, echocardiography may identify changes in the left ventricular size, mass, and wall thickness secondary to physical training that can appear similar to mild dilated or hypertrophic cardiomyopathies. These findings may be accompanied with borderline low left ventricular ejection fraction leading to a diagnosis of cardiomyopathy, but systolic function should appropriately augment under exercise testing in the athletic heart. In addition to properly supervised exercise testing, cardiac MRI (CMR) can help distinguish between pathology and changes related to physical fitness. These diagnostic challenges highlight the importance of ACS evaluation for aviators and special duty personnel with new aeromedical waiver requests for cardiomyopathy.

AIMWITS search in Dec 2019 for the previous five years revealed 41 cases listed as cardiomyopathy. Breakdown of the cases was as follows: 3 FC I/IA (1 disqualified), 18 FC II (1 disqualified), 1 RPA pilot, 14 FC III (4 disqualified), 1 special warfare airman, and 4 ATC/GBC (1 disqualified). All cases with a disqualification either had symptoms, were on a nonapproved medication or did not meet initial flying standards or radiographic evidence of cardiomyopathy.

| ICD-9 Co | ICD-9 Codes for cardiomyopathy   |  |  |
|----------|--|--|--|
| 425.4    | Other primary cardiomyopathies (hypertrophic, restrictive, idiopathic, familial, not otherwise specified, congestive, constrictive, obstructive, nonobstructive) |  |  |
| 425.9    | Secondary cardiomyopathy, unspecified  |  |  |
| 086.0    | Chagas' disease with heart involvement   |  |  |

| ICD-10 Codes for cardiomyopathy |  |  |
|---------------------------------|--|--|
| I42.8                           | Other cardiomyopathies                       |  |
| I42.9                           | Cardiomyopathy, unspecified                  |  |
| B57.0                           | B57.0 Chagas' disease with heart involvement |  |

### IV. Suggested Readings

- 1. D'Arcy JL Manen O, Davenport ED, et. al. Heart Muscle Disease Management in Aircrew. Heart, 2019; 105:s50-s56.
- 2. Nicol ED, Rienks R, Gray G, et. al. An Introduction to Aviation Cardiology. Heart, 2019; 105:s3-s8.
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Foundation/American Heart Association Task Force on Practice Guidelines. Circulation, 2013; 128:e240–e327.

- 4. Maron BJ, Udelson JE, Bonow RO, et. al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis: a scientific statement from the American Heart Association and American College of Cardiology. Circulation, 2015; 132:e273–e280.

## Cataract, Capsular Opacification, and Intraocular Lens Implant (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

For GBO, only disqualifying for RPA, not RPA SO or MOD. MSD C56, C57, C58.

#### I. Waiver Consideration

Opacities, cataracts, or irregularities of the lens, which interfere with vision, or are considered to be progressive, are disqualifying for all flying classes. Pseudophakia (intraocular lens implantation during cataract surgery) and posterior and anterior capsular opacification are disqualifying for Flying Classes I/IA/II, GBO (RPA Pilot duties only), and SWA. For ATC and Operational Support Flying (OSF) duties, pseudophakia and posterior/anterior capsular opacification are not specifically mentioned as a disqualifying diagnosis, but it would become relevant if the vision was impaired. For all classes, no waiver is required if the lenticular opacity is asymptomatic, visually insignificant, and non-progressive (no potential for progression). Per Air Force policy, opacities, cataracts, or irregularities of the lens interfering with vision, render a member unfit for continued service, and require an I-RILO to evaluate for the possibility of retention.

Table 1: Waiver potential for Cataracts, Capsular Opacification, and Intraocular Lens Implant.

| Flying Class<br>(FC)     | Waiver<br>Potential | Waiver<br>Authority | ACS Review or Evaluation      |
|--------------------------|---------------------|---------------------|-------------------------------|
| I/IA                     | No                  | AETC                | No                            |
| $II/III^1$               | Yes                 | AETC or             | Yes <sup>3</sup>              |
| SWA                      |                     | MAJCOM <sup>2</sup> |                               |
| ATC/GBO/OSF <sup>4</sup> | Yes <sup>5</sup>    | MAJCOM              | Only at the request of MAJCOM |

<sup>1.</sup> For initial flying class II and III physicals, waiver is not likely for cataracts deemed potentially progressive. Applicants with a history of cataract surgery will be considered on a case-by-case basis.

<sup>2.</sup> AETC will be the waiver authority for Initial Waivers only; MAJCOMs will be the waiver authority for renewals.

<sup>3.</sup> ACS evaluation required initially after diagnosis of symptomatic/visually significant/progressive cataract or pseudophakia then review only on subsequent renewals.

<sup>4.</sup> Applies to RPA Pilot only, not RPA SO or MOD.

<sup>5.</sup> Pseudophakia and posterior and/or anterior capsular opacification are not disqualifying for ATC and OSF duties.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. Description of any symptoms associated with condition, any noted progression and any prior medical evaluation or treatment for the condition (including operative note, if applicable).
- 2. Comment on location and stability of intraocular lens (IOL), model number, and type of IOL used (if applicable).
- 3. Best corrected visual acuities at distance and near.
- 4. Any contact lens or spectacle correction prescriptions.
- 5. Dilated retinal exam.
- 6. Cone contrast test (CCT) scores for each eye individually.
- 7. Humphrey visual field 30-2 testing for each eye.
- 8. Low contrast acuity testing with Precision Vision 5% acuity chart corrected and uncorrected for each eye.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1. Description of any symptoms associated with condition, any noted progression and any prior medical evaluation or treatment for the condition (including operative note, if applicable).
- 2. Comment on location and stability of intraocular lens (IOL), model number, and type of IOL used (if applicable).
- 3. Best corrected visual acuities at distance and near.
- 4. Any contact lens or spectacle correction prescriptions.
- 5. Dilated retinal exam.
- 6. Cone contrast test (CCT) scores for each eye individually.
- 7. Humphrey visual field 30-2 testing for each eye.
- 8. Low contrast acuity testing with Precision Vision 5% acuity chart corrected and uncorrected for each eye.
- 9 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

**Note:** Aeromedical summaries may not be submitted any earlier than 60 days after extraction and IOL implant. ACS evaluation will not be scheduled until 90 days following the procedure; assuming the aircrew member is stable and off postoperative medications. If just YAG laser surgery is done for a posterior capsule opacification then aeromedical summary may be submitted 30 days after procedure if asymptomatic and off postoperative medications.

#### III. Aeromedical Concerns

Aeromedically, lens changes are defined as *opacities* (developmental lens defects that do not progress) and cataracts (lens opacities with the potential to progress and compromise visual function). Developmental opacities of the lens are not disqualifying, whereas cataracts, including congenital polar cataracts, are. Decreased visual acuity, contrast sensitivity, symptoms of glare, acquired color vision deficiencies, and visual field defects associated with cataracts have the potential to adversely affect mission effectiveness and flight safety. Even if a lens change does not significantly impact vision at present, any of those defined as cataracts have the potential to progress, and some may do so relatively quickly. This progression necessitates, at a minimum, monitoring of any potentially progressive cataract to ensure visual functioning remains unaffected. Some cataractous changes may become problematic only under certain environmental conditions, such as in bright lights or at night.

As with any medical problem in USAF aircrew, medical treatment to meet the current standard of care is mandated without the necessity to receive permission from the ACS or waiver authority. However, there are some complicating issues with cataracts in aircrew. Typically, civilian patients are not operated on until the patient deems his or her vision is poor enough to require surgery. Often this level of severity is after the patient's vision has declined significantly below the 20/20 Air Force vision standard. USAF aircrew may require surgery at an earlier point than their civilian counterparts.

Like any medical condition, implanted IOLs have additional concerns in the aviation environment that are not present in typical daily use. A review of FAA records done in 1993 examined the accident risks for pseudophakic pilots versus phakic pilots. This study found a statistically significant increased risk of aviation mishaps associated with pseudophakic pilots. The risk was even greater for pseudophakic pilots under the age of 50. When compared to their corresponding phakic counterparts, pseudophakic pilots under the age of 50 had 3.72 times the risk of having a mishap while the pseudophakic pilots over the age of 50 had 1.41 times the risk.

Another concern for IOLs is the theoretical risk of dislocation of IOLs under the extreme G-forces in the aviation environment. According to ACS records, there has been no known dislocation of an IOL during flight duties in the USAF. Further, study animals with implanted IOLs were subjected to G-forces up to +12 Gz without any signs of dislocation. A case report in August 2000 demonstrated that IOLs may be stable under high G-forces when a pilot with an IOL ejected from a T-6A Texan and the IOL remained stable.<sup>4</sup>

Only certain IOLs are approved for use in aircrew members. The selection of the procedure and the IOL should be coordinated with the Aeromedical Consultation Service (ACS) [DSN 798-3388, (937) 938-3388] for members on or planning to enter flying status. Generally, the preferred procedure is an extracapsular cataract extraction with implantation of a posterior chamber IOL at either the ciliary sulcus or in the capsular bag. The IOL should be a one piece acrylic IOL or have a three piece design with tissue fixable

haptics (polypropylene [PP], polyethylene [PE] or polymethylmethacrylate [PMMA]) with a 6-7 mm optic and ultraviolet filtering properties. One piece silicone IOLs are <u>not</u> approved for aircrew use because they do not fix well to the capsular bag and silicone material has been found to be pro-inflammatory in the post-operative eye. The multifocal IOLs, accommodating IOLs, and the newer extended range IOLs are also <u>not</u> approved for aircrew use. Finally, any IOLs with plate designs and positioning holes are currently still under review by the ACS.

In Feb 2016, blue blocking IOLs were approved for aircrew use as long as the member can successfully pass the CCT. To date, no aircrew have been disqualified for CCT failure due a blue blocking IOL. Numerous reports have confirmed that blue blocking IOLs have no adverse effects on color vision or contrast sensitivity testing in photopic or mesopic conditions. Additionally, even those with moderate color vision deficiency before surgery showed no change in their color vision after implantation of a blue blocking IOL.

In Aug 2016, toric IOLs were approved for use in aircrew given the advances and long successful record of accomplishment of the IOLs. Patients with corneal astigmatism who receive a toric IOL are twice as likely to not need glasses for distance, have improved visual acuity, improved contrast sensitivity, and only 1.1% experience the complication of requiring a second procedure to realign a rotated IOL. The mean misalignment after toric IOL implantation is 1.1°. By lens model IOL rotation of 5 degrees or less occurred with the Tecnis Toric in 94.2%, MicroSil 6116TU in 90%, Acrysof Toric in 81.1%, and in the Staar Toric AA4203 in 62-73%. The Tecnis Toric and Acrysof Toric are the preferred toric IOLs for aircrew due to their stability and that the MicroSil IOL is made of silicone and the Staar Toric is a plate haptic design.

A Sep 2018 AIMWTS search revealed 347 individuals with the diagnosis of cataract and/or cataract with IOL. Of the total, 13 were FC I/IA cases (11 disqualified), 169 FC II cases (26 disqualified), 3 RPA Pilot cases, 154 FC III cases (33 disqualified), 5 ATC/GBC cases, and 2 MOD cases. There were a total of 70 disqualifications dispositions. Fewer than half of the disqualified cases were directly related to the cataract diagnosis and the majority of individuals were disqualified for additional diagnoses.

| ICD-9 codes for cataract, cataract surgery |                              |  |
|--|------------------------------|--|
| 366  | Cataract                     |  |
| 379.31                                     | Aphakia                      |  |
| 743.30                                     | Congenital cataract          |  |
| V43.1                                      | Lens replaced by other means |  |
| V45.61                                     | Cataract extraction          |  |

| ICD-10 codes for cataract |  |  |
|---------------------------|--|--|
| H25.011-                  | Cataract                                       |  |
| H25.9                     |  |  |
| H26.8                     | Other specified cataract                       |  |
| H26.9                     | Unspecified cataract                           |  |
| H27.0                     | Aphakia, unspecified eye, right eye, left eye, |  |
| 1, 2, 3                   | bilateral                                      |  |
| Q12.3                     | Congenital aphakia                             |  |
| Q12.0                     | Congenital cataract                            |  |

## IV. Suggested Readings

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- 12. Waltz KL, et al. Clinical Outcomes of Tecnis Toric Intraocular Lens Implantation after Cataract Removal in Patients with Corneal Astigmatism. Ophthalmology, 2015; 122: 39-47.

### WAIVER GUIDE

Updated: Aug 2016

Supersedes Waiver Guide of Aug 2012

By: Lt Col Anthony Mitchell (RAM 17), Lt Col Eddie Davenport (ACS chief cardiologist),

and Dr Dan Van Syoc

### **CONDITION:**

Catheter Ablation of Tachyarrhthmias and/or Pre-Excitation (WPW) (Aug 2016)

### I. Waiver Considerations.

Catheter ablation of cardiac tachydysrhythmias is disqualifying for flying class (FC) I/IA, II and III. If catheter ablation is being performed only for aeromedical reasons and not for clinical indications, then ACS review and/or evaluation is highly recommended <u>before</u> RFA to assure that it is aeromedically indicated. The underlying diagnosis may also require a waiver or possible MEB, review the underlying diagnosis waiver guide for further details.

**Table 1: Waiver potential for catheter ablation cases** 

|                             | potential for catheter ablation cases   |                  |                   |
|-----------------------------|---|------------------|-------------------|
| Flying Class                | Condition Treated   | Waiver Potential | ACS               |
|                             | with catheter ablation  | Waiver           | review/evaluation |
|                             |   | Authority**      |                   |
| I/IA                        | WPW ECG pattern   | Yes*             | Yes               |
|                             | only, WPW syndrome and AVNRT  | AETC             |                   |
|                             | Other supraventricular tachycardias to include atrial flutter and RVOT ventricular tachycardia. | Maybe*<br>AETC   | Yes               |
|                             | Atrial fibrillation Ventricular Tachycardia secondary to other cardiac disease process          | No<br>AETC       | No                |
| II/III (including untrained | WPW ECG pattern only  | Yes#<br>MAJCOM   | Yes               |
| applicants)                 | WPW syndrome and AVNRT  | Yes*<br>MAJCOM   | Yes               |
|                             | Other supraventricular tachycardias to include atrial flutter and RVOT ventricular tachycardia. | Maybe*<br>MAJCOM | Yes               |
|                             | Atrial fibrillation   | Maybe+<br>MAJCOM | Yes               |
|                             | Ventricular Tachycardia secondary to other cardiac disease process                              | No               | No                |

<sup>#</sup> No observation post-ablation required prior to waiver submission.

Review of AIMWTS through Mar 2016 for catheter ablation showed 152 cases with 8 total disqualifications. Breakdown of the cases was: 12 FC I/IA cases with 1 disqualification; 83 FC II cases with 2 disqualifications; 48 FC III cases with 4 disqualifications; 5 ATC/GBC cases with 1 disqualification; and 4 MOD cases without any disqualifications.

<sup>\*</sup> Submit waiver 4 months post-ablation observation.

<sup>\*\*</sup> Waiver authority is as listed for the ablation procedure itself. However, if underlying condition required an MEB, waiver authority is AFMRA for FCII, FCIII, ATC, GBO and SWA.

<sup>+</sup> Submit waiver 6 months post-ablation observation.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. If the underlying condition requires an MEB, ensure that the MEB has been completed prior to submitting the waiver.

The AMS for initial waiver should contain the following information:

- A. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- B. Cardiology consult.
- C. Official report of ablation and electrophysiologic study/studies (EPS).
- D. Electrocardiogram (ECG) at 2 months, 3 months and 4 months post-RFA for all tachyarrhythmias. A-fib requires an addition ECG at 6 months.
- E. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)

The AMS for waiver renewal should contain the following information:

- A. History brief summary of previous symptoms and treatment, any interval symptoms, medications, and activity level.
- B. Physical blood pressure and cardiac.
- C. Electrocardiogram (ECG).
- D. Additional local cardiac testing is not routinely required for re-evaluation cases followed at the ACS but may be requested in individual cases. If so, the previous ACS evaluation/review will specify details regarding any requested local testing.
- E. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)

Note 1: All studies should be sent electronically through the ECG library. Mailing studies will increase disposition time. However, if necessary, the address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM)

USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

For expediting cases, we recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

Curative therapy of some tachyarrhythmias and/or ventricular pre-excitation by catheter ablation with high success rates and low complication rates, offers the potential to waiver these individuals for initial flight training and return to flying status. Ablation was first performed by surgical interruption of Wolff-Parkinson-White (WPW) accessory pathways. Catheter ablation followed, first with direct current and more recently with radiofrequency energy (RFA) and cryotherapy; the latter often reserved for ablation in close proximity to high risk areas of the heart such as the AV node. By the 1990's, these ablative techniques were being used for curative treatment of WPW accessory pathways, supraventricular tachycardia (SVT) associated with atrioventricular (AV) node reentry, and ventricular tachycardia usually localized to the right ventricular outflow tract (RVOT). It has since been used for the treatment of other supraventricular and ventricular tachyarrhythmias such as atrial fibrillation and ventricular ectopy albeit with much lower success rates.

Joint guidelines were recently published by the American College of Cardiology, American Heart Association and Heart Rhythm Society regarding the management of all supraventricular tachycardias. These guidelines should be followed for all acute tachyarrhythmias in aviators. For long term therapies these guidelines should also be followed in regard to ablation and beta-blocker use however antiarrhythmic medications and non dihydropyridine calcium channel blockers are rarely waiverable for ongoing flight duties. Detailed definitions and criteria for diagnosis of accessory pathways, supraventricular tachyarrhythmias and ventricular tachycardias are also addressed elsewhere in the waiver guide. Waiver guidelines for these conditions without catheter ablation are addressed in their respective waiver guides. This waiver guide chapter specifically addresses the use of ablation for accessory pathways (such as WPW), SVT associated with AV node reentry, other SVT mechanisms, atrial flutter, atrial fibrillation, and ventricular tachycardias.

#### A. SUPRAVENTRICULAR TACHYARRHYTHMIAS

1. Accessory pathways. These accessory pathways conduct impulses between the atria and ventricles, WPW being the most common type. WPW electrocardiogram (ECG) pattern is the classic ECG findings of short PR interval and delta wave but without documented or suspected SVT. WPW syndrome is the ECG findings plus suspected or documented SVT. About 30% of all SVTs involve an accessory pathway. According to the general cardiac literature, the WPW ECG pattern occurs in 1-3 per 1,000 of the population and an estimated 30-35% will develop a symptomatic arrhythmia during their lifetime. Atrial fibrillation with rapid ventricular response and very high rates of SVT secondary to retrograde conduction, deteriorating into ventricular fibrillation, is considered the likely cause of sudden death. Recent review of the ACS ECG library database showed much lower rates of SVT and SCD and therefore ablation should be reserved for high risk pathways or confirmed WPW syndrome, and not simply ventricular pre-excitation which is commonly referred to as WPW pattern (see WPW waiver guide). Catheter ablation is potentially curative for accessory pathway tachyarrhythmias with an

immediate success rate of 95-99%. Most recent guidelines recommend catheter ablation particularly, if the accessory pathway has a short refractory period that allows rapid antegrade conduction. However, recurrence of a functional accessory pathway occurs in 1-5%, usually within 2-4 months after ablation. Late recurrence is rare.

- 2. Atrioventricular node reentrant tachycardia (AVNRT). AVNRT is the most common mechanism of SVT (about 60% of all SVT cases). It is caused by a reentry circuit within the AV node. The published experience on catheter ablation for AVNRT is comparable to that of WPW ECG pattern and syndrome, with a success rate approaching 99% and a recurrence rate of 1-2%.
- 3. Other supraventricular tachycardias. The remaining 10% of SVTs are due to a variety of uncommon mechanisms. These may include reentrant pathways and automatic foci, such as automatic atrial tachycardia and paroxysmal junctional tachycardia. Published experience of ablation regarding these rhythm disturbances is limited.
- 4. Atrial flutter. Atrial flutter is due to a localized reentry circuit in the right atrium near the tricuspid valve. Curative ablation is very feasible, with success rates matching those of accessory pathways and AVNRT. However, atrial flutter can often be associated with atrial fibrillation and residual atrial fibrillation complicates successful atrial flutter ablation. Careful review of actual electrophysiologic testing, ablation procedure, and chart review is necessary for prognostication.
- 5. Atrial fibrillation (AF). Lone AF does not mean a single episode of AF. Rather it means idiopathic AF. Lone AF is usually defined as no underlying structural heart disease, hypertension, or hyperthyroidism and age younger than 60 years at time of diagnosis. RFA may be curative for the subset of paroxysmal or chronic lone AF individuals who have one or a few triggering arrhythmogenic sites, most commonly in or near the pulmonary vein ostia. The reported success rates range from 50-80%, much lower than for ablation of WPW or AVNRT. And many of these individuals required one or more repeat ablations to effect a cure. Most centers performing atrial fibrillation ablation do so for quality of life issues – poor control to at least 1 class I or II antiarrhythmic medications, medications or unacceptable symptoms from the rhythm or medications. Successful ablation may then be defined as control of the AF on continued medications but with no or acceptable symptoms/side effects. This would not be an acceptable endpoint for all flying classes. Absence of atrial fibrillation without need for medications would be the desired aeromedical result. There is limited published experience regarding long-term outcomes of RFA of AF. Several procedures have been used; success rates and complications depend partly on the specific technique.

#### B. VENTRICULAR TACHYCARDIA

Ventricular tachycardia (VT) is defined as three or more consecutive ventricular beats at a rate of 100 beats per minute or faster. Guidelines for VT without ablation are addressed in the ventricular tachycardia waiver guide. Most published experience with ablation for VT deals with ablation performed for sustained VT or hemodynamically symptomatic

nonsustained VT, often in the setting of failure of one or more antiarrhythmic medications. Recurrence rates post-RFA vary in the clinical literature from 0% to 30% within 1-2 years. In many reports control of VT on antiarrhythmic medications is considered an ablation cure. Long-term success, outcomes, recurrence rates and late adverse consequences of the several mechanisms of VT are not well described in the literature. There are several mechanisms for VT and ablation cure rates are very dependent on the VT mechanism and location within the ventricles, as well as presence or absence of underlying cardiac pathology. Most published success rates range between 50% and 75% at 6 to 12 months but very little is known beyond this time frame. Only ablation of idiopathic VT (no underlying cardiac pathology) may be favorably considered for waiver.

### IV. Aeromedical Concerns.

Sudden cardiac death is the most compelling concern; however, in many tachyarrhythmias this risk is low. The risk of recurrent sustained tachyarrhythmia and associated hemodynamic symptoms is the more likely aeromedical concern. To quantify these risks, the specific tachyarrhythmia, the presence or absence of hemodynamic symptoms and results of electrophysiologic studies and/or RFA must be considered. Careful review of the ablation procedure and corresponding electrophysiologic study is paramount as this will provide details of the mechanisms and characteristics of the ablated pathway. These characteristics as well as response to ablation acutely will provide prognostic information necessary for aeromedical disposition. See individual waiver guides for more details on each specific diagnosis.

| ICD-9 Code for radiofrequency ablation procedure |                         |  |
|--|-------------------------|--|
| 37.34  | Radiofrequency ablation |  |

| ICD-9 Codes for conditions requiring catheter ablation |  |  |
|--|--|--|
| 426.7  | Anomalous atrioventricular excitation (Wolff-Parkinson-White |  |
|  | syndrome)  |  |
| 427.0  | Paroxysmal supraventricular tachycardia                      |  |
| 427.1  | Ventricular tachycardia                                      |  |
| 427.31   | Atrial fibrillation  |  |
| 427.32   | Atrial flutter   |  |

| ICD-10 Codes for conditions requiring catheter ablation |  |  |
|---|--|--|
| I45.89  | Anomalous atrioventricular excitation (Wolff-Parkinson-White |  |
| I45.6   | syndrome)  |  |
| I47.1   | Paroxysmal supraventricular tachycardia                      |  |
| I47.2   | Ventricular tachycardia                                      |  |
| I48.91  | Atrial fibrillation  |  |
| I48.82  | Atrial flutter   |  |

#### V. References.

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- 2. Kruyer WB, Davenport ED. Cardiology. In: *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed. New York: Graduate Medical Publishing, LLC, 2013; 47-70 and 49-56.
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- 7. Stevenson WG and Tedrow U. Preventing ventricular tachycardia with catheter ablation. Lancet, 2010; 375: 4-6.

## Celiac Disease (Apr 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

Significant Changes: Waiver guide restructured.

### I. Waiver Consideration

Celiac disease (CD) is disqualifying for all flying and special operational duties as well as retention. Additionally, any malabsorption syndrome requiring a specialized diet that is not compatible with prolonged subsistence on MREs is disqualifying for all flying and special operational duties as well as retention. Initial aeromedical waiver for trained aircrew, ground based operators, and special duty operators can be considered once an individual has demonstrated tolerability of a gluten free diet and initial presenting symptoms have resolved. Untrained personnel with a confirmed diagnosis of CD are generally felt to have poor waiver potential.

Table 1: Waiver potential for Celiac disease.

| Flying Class<br>(FC)     | Waiver<br>Potential <sup>1,2</sup> | Waiver<br>Authority | ACS Review or<br>Evaluation |
|--------------------------|------------------------------------|---------------------|-----------------------------|
| I/IA                     | No                                 | AETC                | No                          |
| II/III<br>ATC/GBO<br>SWA | Yes                                | MAJCOM              | Yes                         |

<sup>1.</sup> Untrained personnel in any category are unlikely to receive aeromedical waiver and ACS review/evaluation is not necessary.

### II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

### A. Initial Waiver Request:

- 1 Summary of presentation, course, and treatment.
- 2 Consultation reports form all treating provider or specialists, which should include:
  - a Description of clinical symptoms and if these symptoms have resolved with gluten free diet.
  - b. Subjective symptoms and objective physical exam findings to include thorough skin exam.
  - c Documentation reporting how the diagnosis was made including any esophagogastroduodenoscopy (EGD) reports, pathology reports, or Celiac serology studies that are available.

<sup>2.</sup> Symptoms must be well controlled with gluten free diet (GFD) and operational demands must allow for reliable access to GFD.

d Assessment for adherence to gluten free diet and degree of symptom improvement.

# 3 Laboratory studies required:

- a CBC and LFTs
- b All other laboratory and imaging studies ordered by treating provider(s) or consulting specialist(s), if performed. These results may include serology studies such as IgA tissue transglutaminase antibody (tTG), IgA deamidated gliadin peptide (DGP), IgA endomysial antibody (EMA), or total IgA levels or esophagogastroduodenoscopy (EGD) with biopsy and pathology reports.
- 4 Current physical examination findings.
- 5 FL4 with RTD and ALC status.
- 6 Any other pertinent information.
- 7 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including: Summary of presentation, course, and treatment.
- 2 Consultation reports form all treating providers or specialists, which should include:
  - a Subjective symptoms and objective physical exam findings to include full skin examination
  - b Assessment of adherence to gluten free diet
- 3 Laboratory studies required:
  - a. Updated CBC
  - b. All other laboratory and imaging studies ordered by treating providers or consulting specialist(s), if performed
- 4 Current physical examination findings.
- 5 Any other pertinent information.
- 6 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Celiac disease is an autoimmune disease primarily causing intestinal symptoms; however, extra-intestinal symptoms are not uncommon. Intestinal symptoms include abdominal discomfort, bloating, diarrhea, and weight loss due to malabsorption. Depletion of vitamins and nutrients from malabsorption potentially results in anemia, peripheral neuropathy, and osteoporosis. Anemia and peripheral neuropathy potentially result in subtle performance decrement due to hypoxemia at altitude or loss of fine motor dexterity, respectively. Extra-intestinal symptoms include fatigue, headaches, neuropathy, neuropsychiatric disturbances, and rash (dermatitis herpetiformis). Rarely, occult gastrointestinal malignancies develop. Celiac disease may be associated with other autoimmune conditions such as type 1 diabetes mellitus and Hashimoto's thyroiditis. Although Celiac disease is unlikely to result in sudden incapacitation, intestinal and extra-intestinal manifestations potentially could interfere

with daily operational duties. A gluten free diet is the only validated method to ensure control of symptoms. Per the AFI 48-123, special handling or severe dietary restrictions is a retention issue given the limited dietary options in deployed and austere environments were members do not have direct control over their dietary sources. Recurrence of symptoms is often due to poor dietary adherence or incidental exposure to gluten.

Review of AIMWTS data in Apr 2019 revealed a total of 25 waiver packages containing the diagnosis of Celiac disease since Jan 2014. Of that total, 0 were FC I/IA, 12 were FC II (0 disqualified), 5 were FC III (0 disqualified), 1 were ATC/GBC (0 disqualified), and 1 were MOD (0 disqualified).

| ICD-9 codes for Celiac Disease |                |  |
|--------------------------------|----------------|--|
| 579.0                          | Celiac Disease |  |

| ICD-10 codes for Celiac Disease |                |  |
|---------------------------------|----------------|--|
| K90.0                           | Celiac Disease |  |

## **IV. Suggested Readings**

- 1. Freeman, HJ. Adult Celiac Disease and Its Malignant Complications. *Gut and Liver*. 2009; 3(4):237-246.
- 2. Leonard MM, Sapone A, Catassi C and Fasano A. Celiac Disease and Nonceliac Gluten Sensitivity: A Review. *JAMA*. 2017; 318(7):647-656.
- 3. Rubio-Tapia A, Hill ID, Kelly CP et al. ACG Clinical Guidelines: Diagnosis and Management of Celiac Disease. *American Journal of Gastroenterology*. 2013; 108:656-676. https://gi.org/guideline/diagnosis-and-management-of-celiac-disease/

### **Central Retinal Vein Occlusion (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

New Ground Based Operator (GBO) Standards. MSD C43, C46.

#### I. Waiver Consideration

Central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) are disqualifying for Flying Class I, IA, II, III, and SWA duties. For ATC, GBO, and Operational Support Flying Duty (OSF) personnel, these conditions would be disqualifying if there are residual visual symptoms such as loss of visual acuity, visual field defects, or loss of color vision below standards. An Aeromedical Consultation Service (ACS) evaluation is required for aviators for all initial waivers for CRVO/BRVO. The probability of waiver approval is dependent on the final visual acuity, visual field, and absence of other significant pathology or complications. Any underlying contributing pathology must also be waiverable for the individual to be returned to flight status. For waiver renewals, ACS review is required. Depending on the results of local work-up, an ACS evaluation may be required prior to waiver renewal.

**Table 1: Waiver potential for Retinal Vein Occlusion** 

| Flying Class | Waiver Potential      | Waiver Authority | ACS                      |
|--------------|-----------------------|------------------|--------------------------|
| (FC)         |                       |                  | <b>Evaluation/Review</b> |
| I/IA         | Maybe <sup>1, 2</sup> | AETC             | Yes                      |
| II/III       | Yes <sup>2</sup>      | MAJCOM           | Yes                      |
| SWA          |                       |                  |                          |
| ATC/GBO/OSF  | Yes <sup>2, 3</sup>   | MAJCOM           | At the discretion of the |
|              |                       |                  | waiver authority         |

<sup>1</sup> No waiver potential for RVO with residual visual defects in initial FC I/IA applicants.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

<sup>2</sup> Visual outcome needs to have returned to baseline without presence of any recognized risk factors. The Waiver Authority for untrained aircrew is AETC.

<sup>3</sup> Waiver only required if RVO residual symptoms are disqualifying (visual field defect, color vision loss, etc.)

## A. <u>Initial Waiver Request:</u>

- 1. Consideration of any potentially underlying disease etiologies, to include hypertension, heart disease, diabetes, hematologic disease, or collagen vascular disease with appropriate work-up and lab testing results.
- 2. List and fully discuss all clinical diagnoses requiring a waiver.
- 3. History of disease, including treatment modalities attempted.
- 4. Full ophthalmology exam to include:
  - a. Presence or absence of any visual symptoms.
  - b. Best corrected visual acuities at distance and near.
  - c. Examination of fellow eye with pertinent findings.
  - d. Cone contrast testing (CCT) for each eye.
  - e. Best corrected 5% Precision Vision (low contrast) acuity testing, if available.
  - f. Humphrey visual field 30-2 and 10-2 testing for each eye, if available.
  - g. Specialist report must comment on the presence or absence of macular edema, retinal hemorrhage, neovascularization, and glaucoma. Include Optical Coherence Tomography and/or Fluorescein Angiography, if available.
- 5. Lab testing results for fasting blood glucose, A1C, CBC + differential, PT/PTT, ESR, CRP, Lipids, ANA, Treponemal AB, and homocysteine.
- 6. If the local base cannot provide all of the above information, an explanation needs to be given to the MAJCOM as to why not.

# B. Renewal Waiver Request:

- 1 Interim history since last waive and ACS visit.
- 2 Ongoing treatment modalities
- 3 Full ophthalmology exam to include items as noted above.
- 4 If the local base cannot provide all of the above information, an explanation needs to be given to the MAJCOM as to why not.
- Note: if above items are not available, member must come for full ACS evaluation.

#### III. Aeromedical Concerns

The primary aeromedical concerns with CRVO/BRVO are loss of best-corrected visual acuity, loss of visual field, decreased night vision, loss of color vision, loss of low contrast vision, and loss of stereopsis. Other concerns include persistent complications such as neovascular glaucoma, macular edema, as well as ensuring proper management of any predisposing medical conditions. The risk of BRVO developing in the non-affected eye is approximately 10% within three years of initial presentation. The risk of fellow eye involvement in CRVO cases is 1% per year based on published data. A common complication following RVO is the development of neovascular glaucoma in eyes with ischemic CRVO, which approaches 40% over one year. Persistent, chronic macular edema is not waiverable due to the risk of worsening of this condition during flight and associated reduced visual function. Even if vision is adequately restored to meet vision standards, the underlying systemic conditions leading to RVO may pose potential serious risks to safe flight. Therefore, investigation of the underlying cause is critical to both management and aeromedical disposition. Also of aeromedical concern is exposure to the

hypoxic environment of altitude. A small case report series discussed the implications of high-altitude as a possible cause to RVO. Though these patients were typically exposed to the high-altitude environment for several weeks, one patient did develop BRVO while driving to altitude. These occurrences create some concern specifically for recurrence of events especially in light of literature suggesting decreased oxygen saturation in the venous circulation of the retina up to three months following the acute event.

AIMWTS review in Jan 2019 revealed 24 cases containing the diagnosis of retinal vein occlusion. There were no FC I/IA cases, 14 FC II cases and 10 FC III cases. There were three cases disqualified, one FC II and two FC III.

| ICD 9 Codes for Retinal Vein Occlusion |                                       |  |  |
|--|---------------------------------------|--|--|
| 362.35                                 | 362.35 Central Retinal Vein Occlusion |  |  |
| 362.36                                 | Branch Retinal Vein Occlusion         |  |  |

| ICD-10 Codes for Retinal Vein Occlusion |  |  |
|---|--|--|
| H34.81                                  | Central Retinal Vein Occlusion, Right, Left, |  |
| 1, 2, 3, 9                              | Bilateral, Unspecified                       |  |
| H34.83                                  | Branch Retinal Vein Occlusion, Right, Left,  |  |
| 1, 2, 3, 9                              | Bilateral, Unspecified                       |  |
| H34.9                                   | Unspecified Retinal Vascular Occlusion       |  |

## **IV. Suggested Readings**

- 1. Ehlers JP and Fekrat S. Retinal Vein Occlusion: Beyond the Acute Event. Surv Ophthalmol, 2011; 56(4): 281-299. 53(2): 112-20.
- 2. Hardarson SH and Stefánsson E. Oxygen Saturation in Central Retinal Vein Occlusion. Am J Ophthalmol, 2010; 150(6): 871-75.
- 3. Gupta A, Singh S, Ahluwalia TS, and Khanna A. Retinal Vein Occlusion in High Altitude. High Altitude Med Bio, 2011; 12(4): 393-97.

### **Central Serous Chorioretinopathy (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** New Ground Based Operator (GBO) Standards. Oral eplerenone can speed recovery of CSR. Half dose photodynamic therapy should be considered for members who do not respond to oral eplerenone. MSD C43.

#### I. Waiver Consideration

Central Serous Chorioretinopathy (CSR) is disqualifying for all FC I/IA, II, III, and SWA duties and requires ACS evaluation for waiver consideration. CSR is not specifically disqualifying for ATC, GBO (RPA Pilot, RPA SO, and MOD), and OSF duties, but will be disqualifying if it results in visual acuity problems or significantly alters color vision. Although CSR is not disqualifying for these members, they should still get referred to an ophthalmologist for diagnosis and treatment to speed resolution and ensure preservation of good vision. After documented resolution of CSR by a fundus exam and optical coherence tomography (OCT), a waiver may be requested. Even if the aviator's vision returns to 20/20 or is correctable to 20/20, a local eye specialist must demonstrate that the sub-retinal fluid has resolved prior to waiver request submission. Waivers may be requested for aviators with best-corrected vision less than 20/20 or residual visual symptoms (metamorphopsia, color vision deficits), however, the visual acuity and visual symptoms must be stable (not improving or worsening). If photodynamic therapy (PDT) or laser photocoagulation is performed, the airman must remain DNIF for 30 days following the procedure and requires a full local ophthalmologic exam to include a dilated fundus exam and Humphrey visual field 30-2 testing prior to waiver request submission. The eye exam must demonstrate resolution of the sub-retinal fluid by fundus exam and OCT. If CSR recurs in an aviator with a known history of prior CSR, it is treated the same as an initial occurrence. The aviator will require a new waiver request to be submitted prior to return to flight status with a possible ACS review/evaluation.

Current literature supports initiating oral mineralocorticoid receptor antagonists (spironolactone or eplerenone) earlier after diagnosis to speed recovery. <sup>1,2,3</sup> Given the side effect profile of spironolactone, eplerenone use is preferred and should be started at a dose of 50 mg daily for one week and then increased to 50 mg BID until fluid resolves (typically 1-2 months). Once the fluid is resolved, eplerenone may be tapered to daily for one to two weeks and then stopped. Hyperkalemia is a known side effect and potassium levels should be monitored for any member who requires eplerenone use longer than two months in duration. Members who do not respond to medical treatment should be considered for half-dose photodynamic therapy (PDT).

**Table 1: Waiver potential for Central Serous Chorioretinopathy.** 

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS<br>Review/Evaluation |
|-------------------|------------------|------------------|--------------------------|
| I/IA              | No               | AETC             | No                       |
| II/III/SWA        | Yes <sup>1</sup> | MAJCOM           | Yes                      |
| ATC/GBO/OSF       | N/A              | N/A              | N/A                      |

<sup>1.</sup> Waiver in untrained FC II and III individuals is unlikely but will be considered on a case-by-case basis.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

## A. <u>Initial Waiver Request:</u>

- 1. Complete history of symptoms (negatives included), medical or laser treatment, and residual visual complaints.
- 2. Medical History including possible contributing factors such as steroid use, HCTZ use, or Obstructive Sleep Apnea.
- 3. Attach studies (optical coherence tomography [OCT], fluorescein angiograms [FA] or indocyanine green angiograms) if performed.
- 4. Full ophthalmology exam to include:
  - a. Documentation of resolution of CSR by fundus exam and an OCT.
  - b. Documentation of visual acuities at or better than 20/20 in each eye or documented stability of a visual acuity less than 20/20.
  - c. Results from Amsler grid testing.
  - d. Results of CCT for each eye individually.
  - e. OVT-DP results, if not within standards then AO Vectograph results.
- f. Humphrey visual field 30-2 testing for each eye if laser photocoagulation was performed (waiver request may not be submitted until 30 days after the procedure).
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority

### B. Renewal Waiver Request:

- 1 A brief medical history summarizing the initial occurrence of the CSR, any recurrences and any treatment, as well as a full description of any residual visual complaints.
- 2 Full ophthalmology exam to include:
  - a. Documentation of continued resolution of CSR by fundus exam and an OCT.
  - b. Visual acuity in each eye, uncorrected and corrected.
  - c. Results from Amsler grid testing.
  - d. CCT scores from each eye individually.
- If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

#### III. Aeromedical Concerns

Normal visual function is crucial in the aerospace environment. Central serous chorioretinopathy (CSR) can adversely impact visual function with symptoms of metamorphopsia (distortion of vision), micropsia (smaller visual images), scotomata (areas of the visual field missing or blurred), blurred vision, color desaturation (reduced brightness of colors), or sub-standard visual acuity. A 1988 Aeromedical Consultation Service (ACS) study that examined 47 rated airmen with 55 eyes affected by CSR found that all but one of the patients was returned to flying status. Fifty-one percent of airmen had recurrent episodes, 86% had better than 20/20 visual acuity after resolution of the CSR, 87% had normal color vision and 90% had normal stereopsis. A current study is pending legal review and IRB approval to review the current outcomes of the CSR Management Group.

The effect of the aerospace environment on active CSR is currently unknown. The presence of sub-retinal fluid introduces new dynamics into the eye that are not present otherwise. The effect of applying G-forces or relative hypoxia upon the pathophysiologic process of CSR is unclear. Further, sub-retinal fluid indicates active disease, which introduces the possibility of fluctuating visual acuity and could have an adverse impact on flight safety. Because of the aeromedical implications of these variables, aircrew members will not be considered for return to flight status until complete resolution of the sub-retinal fluid occurs as demonstrated by ophthalmologic exam and ancillary studies.

For aircrew members that have a history of CSR, regular follow-up care and monitoring are critical for flight safety and continued ocular health. If contributing medical factors such as steroid use, HCTZ use, or a history of Obstructive Sleep Apnea are identified, these should be addressed to minimize recurrences and to hasten resolution of the subretinal fluid. Self-administered Amsler grid testing is the primary method for aircrew to assess for recurrence or worsening of CSR. Aircrew members should obtain an Amsler grid from the local optometrist office and test each eye individually daily for the first year following the CSR. Any new distortion of the lines (metamorphopsia) or missing parts of lines (scotomas) should be immediately reported to the local flight surgeon with subsequent referral to ophthalmology. If no recurrence has occurred within the first year, then weekly Amsler grid testing is appropriate. In addition to Amsler self-testing, aircrew members with a history of CSR require annual full local ophthalmology evaluations as follow-up. These exams should specifically note visual acuity, Amsler grid testing, OVT depth perception testing, CCT color testing, and dilated funduscopic examination results. The result of these exams should be included in the AMS with submission for waiver request.

AIMWTS search in Jan 2019 revealed 164 members with a diagnosis of CSR. Breakdown of the cases reveals: 3 FC I/IA cases (3 disqualified), 98 FC II cases (8 disqualified), 5 RPA pilot cases (1 disqualified), 55 FC III cases (9 disqualified), and 3 ATC/GBC cases (1 disqualified).

| ICD-9 code for central serous chorioretinopathy |                            |  |
|---|----------------------------|--|
| 362.41  | Central serous retinopathy |  |

| ICD-10 code for central serous chorioretinopathy |                            |  |  |
|--|----------------------------|--|--|
| H35.71 Central serous retinopathy, right, left,  |                            |  |  |
| 1, 2, 3, 9                                       | bilateral, unspecified eye |  |  |

# **IV. Suggested Readings**

- Bousquet E, et al. Mineralocorticoid Receptor Antagonism in the Treatment of Chronic Central Serous Chorioretinopathy: A Pilot Study. Retina 2013; 33:2096-2102.
- 2. Zucchiatti I, et al. Eplerenone Versus Observation in the Treatment of Acute Central Serous Chorioretinopathy: A Retrospective Controlled Study. Ophthalmol Ther 2018; 7:109-118.
- 3. Kapoor KG and Wagner AL. Mineralocorticoid Antagonists in the Treatment of Central Serous Chorioretinopathy: A Comparative Analysis. Ophthalmic Res 2016; 56:17-22.
- 4. Green RP, Carlson DW, Dieckert JP, and Tredici TJ. Central Serous Chorioretinopathy in US Air Force Aviators: A review. Aviat Space Environ Med, 1988; 59(12): 1170-75.

## **Cervical Cancer (Jun 2019)**

Reviewed: Maj David Leary (RAM 20), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), Lt Col Jason Massengill (AF/SG OB/GYN consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Updates reflective of changes in DoDI 6130.03, the MSD, and the new Waiver Guide format.

#### I. Waiver Consideration

In trained aviators, abnormal PAP tests are not disqualifying and do not require DNIF unless the flyer has physical or emotional symptoms that warrant grounding until resolved, as determined by their flight surgeon. IAW DoDI 6130.03, new accessions with abnormal cervical cytology within the preceding 3 years (excluding atypical squamous cells of undetermined significance [ASCUS] with human papilloma virus [HPV] and confirmed low-grade squamous intraepithelial lesions [LSIL]) are disqualified for service entry, as is any history of malignancy. All malignant neoplasms (i.e. cancer) require I-RILO processing and are disqualifying for aviation duties. Cervical carcinomas-in-situ with no sequelae after surgical cure are exempt from this requirement.

In general, aeromedical waivers are granted for cervical cancers, after meeting all requirements. The one exception is stage IVB disease (distant metastasis), which remains non-waiverable.

**Table 1: Waiver potential for Cervical Cancer** 

| Flying Class (FC) | Disease/Condition | Waiver<br>Authority<br>Waiver Potential | ACS<br>Review/<br>Evaluation |  |
|-------------------|-------------------|---|------------------------------|--|
| EC I/IA           | Stages IA1 – IIA  | AETC<br>Yes 1, 4                        | Yes                          |  |
| FC I/IA           | Stages IIB – IVB  | AETC<br>No                              | No                           |  |
| FC II/III         | Stages IA1 – IVA  | MAJCOM<br>Yes <sup>2, 3, 4</sup>        | Yes                          |  |
| ATC/GBO/SWA       | Stage IVB         | MAJCOM<br>No                            | No                           |  |

- 1. For FC I/IA individuals, waiver may be considered after 5 years of remission and are asymptomatic.
- 2. For trained personnel waiver may be considered six months after treatment completed and are in remission and asymptomatic.
- 3. For untrained personnel, waiver may be considered after 5 years of remission.
- 4. No indefinite waivers.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### A. <u>Initial Waiver Request:</u>

- 1. Summary of presentation, course, and treatment.
  - a. Include: symptoms; pathology; stage; treatment: including date of last treatment, surveillance plan and activity level.
- 2. Current physical examination findings (including but not limited to genital and rectovaginal exam, lymph nodes, abdomen, etc.)
- 3. Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated).
  - a. Include all follow-up PAP results, frequency per National Comprehensive Cancer Network (NCCN) guidelines.
  - b. Any initial and follow-up labs (minimum of CBC and BUN/Creatinine levels)
- 4. Any consultation reports, including follow-up notes with examination findings after disease resolution.
  - a. Gynecology/Oncology consult reports to include the six-month follow-up visit in accordance with the NCCN guidelines.
  - b. Include tumor board report (military or civilian) if applicable.
- 5. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 6. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 7. Medical evaluation board results (FL4 with RTD and ALC status, if member did not meet retention status)
- 8. Any other pertinent information.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1 Interim history since last waiver submission.
- 2 Physical exam should include but is not limited to: genital, rectovaginal exam, lymph nodes, and abdomen.
- 3 Any consultation reports (i.e. Gynecology/Oncology), including follow-up notes with examination findings after disease resolution.
  - a. Gynecology/Oncology consult reports to include the six-month follow-up visit in accordance with the NCCN guidelines.
  - b. Include tumor board report (military or civilian) if applicable.
- 4 Reports of any pertinent laboratory studies, imaging studies, copies of images since last waiver.
  - a. Include all follow-up PAP results (frequency per NCCN guidelines)
  - b. Any follow-up labs

- 5 Discuss the status of any previously identified treatment complications. Include a discussion of any new complications that developed since the previous waiver. Include information on the functional impact of these complications and the management plan.
- 6 Any other pertinent information.
- 7 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Cervical cancer is the most common cancer caused by a known preventative cause in the United States, and is associated with an infection of the human papilloma virus (HPV), with serotypes 16, 18, 31, 33, 45, and 56 responsible for more than 80% of invasive cervical cancers. Symptoms depend on location and extent of spread of the cancer, but can minimally include invasion of the cervical tissue (causing irregular vaginal bleeding) or can include extension into the surrounding tissue/organs of the vagina, bladder, and GI tract. Risk factors for cervical cancer include early age at first intercourse (age 13 years or younger), multiple sexual partners, multiparity, lower socioeconomic standing, cigarette smoking, history of sexually transmitted diseases, and immunosuppression (e.g. HIV positive, organ transplant patients, and long-term corticosteroid use). Treatment for cervical cancer depends on the stage of the disease, but can include surgical excision, chemotherapy, and/or radiation therapy. The 5-year survival rate for all stages of cervical cancer is close to 68%, but if caught in the early (local) stages 5-year survival exceeds 90%. Complications from treatment for cervical cancer vary depending on the type of treatment (for example, radiation therapy can cause inflammatory reactions like proctitis, ulcerations, strictures, etc.) which all need to be considered when deciding whether a flyer is ready for a return to fly recommendation.

The U.S. has seen a declining trend over the past 10 years in the number of new cervical cancer cases diagnosed, which has been attributed to the widespread use of primary prevention strategies (sexual abstinence, condom usage, and HPV vaccination) and secondary prevention strategies (improvements in evidence-based screening involving PAP test, cervical cytology and HPV screening).

#### **Bottom Line:**

Cervical cancer is highly preventable utilizing primary prevention recommendations like HPV vaccination and safer-sex practices. When caught early, through focused secondary prevention (screening), cervical cancer treatments have a high rate of success, and the likelihood of returning to flying is high. Success of treatment declines as the stage that the cancer is diagnosed increases. It is important to remember that cancer diagnoses of any type may lead to emotional distress and the member's mental health and emotional wellness need to be adequately assessed and appropriately managed prior to considering a return to fly decision.

Following treatment, the aeromedical concerns primarily surround the sequelae of treatment, the logistics of surveillance, and the potential for local or metastatic disease

recurrence. The level of concern increases with advancing stages of disease, and each case needs to be evaluated individually.

Review of AIMWTS data through April 2019 revealed 11 cases of cervical cancer requiring aeromedical waivers. In the past five years, only 4 waivers were required, all of which were granted.

| ICD-9 codes for Cervical Cancer             |  |  |
|---|--|--|
| Malignant neoplasm of the cervix uteri      |  |  |
| 233.1 Carcinoma in situ of the cervix uteri |  |  |

| ICD-10 codes for Cervical Cancer |  |  |
|----------------------------------|--|--|
| C53.0                            | Malignant neoplasm of the endocervix                   |  |
| C53.1                            | Malignant neoplasm of the exocervix                    |  |
| C53.8                            | Malignant neoplasm of overlapping site of cervix uteri |  |
| C53.9                            | Malignant neoplasm of the cervix uteri, unspecified    |  |

### **IV. Suggested Readings**

- 1. <a href="http://www.cdc.gov/cancer/cervical/pdf/guidelines.pdf">http://www.cdc.gov/cancer/cervical/pdf/guidelines.pdf</a>. Accessed 17 Apr 2019.
- 2. http://seer.cancer.gov/statfacts/html/cervix.html. Accessed 17 Apr 2019.
- 3. Cervical Cancer. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology; V.4.2019.

https://www.nccn.org/professionals/physician\_gls/pdf/cervical.pdf

- 4. Massad S, Einstein MH, Huh WK, et al. 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors. J Lower Genital Tract Dis, 2013; 17(5): S1-S27.
- 5. Feldman S, Goodman A, and Peipert J. Screening for cervical cancer. UpToDate Apr 2, 2019.
- 6. Straughn JM and Yashar C. Management of early-stage cervical cancer. UpToDate Nov 8, 2018.
- 7. Waxman AG and Zsemlye MM. Preventing Cervical Cancer: The Pap Test and the HPV Vaccine. Med Clin N Am, 2008: 92: 1059-82.
- 8. Petignat P and Roy M. Diagnosis and management of cervical cancer. BMJ, 2007; 335: 765-68.
- 9. Castle PE, Sideri M, Jeronimo J, et al. Risk assessment to guide the prevention of cervical cancer. Am J Obstet Gynecol, 2007; 197: 356e1-e6.
- 10. Frumovitz, M. Invasive cervical cancer: Epidemiology, risk factors, clinic manifestations, and diagnosis. UpToDate Dec 7, 2018.

### Cholesteatoma (Feb 2019)

Reviewed: Lt Col Marshall Hayes (RAM 20), Dr. Dan Van Syoc (Deputy Chief, ACS), Lt Col Wesley Abadie (AF/SG consultant for otolaryngology) and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

New Format

#### I. Waiver Consideration

History of cholesteatoma or history of surgical removal of cholesteatoma is specifically disqualifying for flying classes I/IA, II, III, as well as for OSF, and SWA duties. Cholesteatoma is not specifically disqualifying for GBO or ATC duties in the MSD, unless it is associated with otitis media or mastoiditis that interferes with satisfactory job performance or requires more than annual specialist follow up, or results in H-3 or worse hearing. Due to the requirement for long-term follow-up, it is recommended that initial waivers be limited to one year. Patients with cholesteatoma will require regular and prolonged follow-up with otolaryngology while on flying status. Recurrence is best managed when caught early. Indefinite waivers will be uncommon.

**Table 1: Waiver potential for Cholesteatoma** 

| Flying Class (FC) | Disease/Condition | Waiver Potential Waiver Authority | ACS<br>Review/<br>Evaluation |
|-------------------|-------------------|-----------------------------------|------------------------------|
| FC I/IA           | Cholesteatoma     | Maybe <sup>1,2</sup><br>AETC      | Yes                          |
| FC II/III<br>SWA  | Cholesteatoma     | Yes <sup>1,2</sup><br>MAJCOM      | Yes                          |
| ATC<br>GBO        | Cholesteatoma     | N/A                               | N/A                          |

<sup>1</sup> For FC I/IA, initial FC II/III, surgery for cholesteatoma must have occurred at least two years previous to waiver submission with documentation indicating the cholesteatoma was completely removed; hearing profile must be H-1. AETC is the certification authority for all untrained assets except for MOD candidates which go to AFGSC. Indefinite waiver may be considered for cases that occurred years prior to consideration if there has been no recurrence and hearing is excellent.

2 IFC I/IA candidates need to wait a minimum of two years post treatment before consideration of waiver. For all others, after 6 months, individuals must demonstrate normal eustachian tube function (i.e., a normal valsalva), and a stable or waiverable hearing profile (if a conductive hearing loss is present). For non-trained assets an H-2 hearing profile requires waiver submission, and for trained assets an H-3 requires waiver. Individuals will need close otolaryngology/flight surgeon observation during the first year post-op.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

# A. <u>Initial Waiver Request:</u>

- 1. History of risk factors (i.e., eustachian tube dysfunction, pressure equalization (PE) tubes, age at first and subsequent PE tube placement, a history of other ear surgeries, episodes of otitis media, smoking status, etc.). Symptoms, including pertinent negatives, should be addressed, (e.g., dizziness, vertigo, facial paralysis, eustachian tube dysfunction, etc., treatments, and prognosis).
- 2. Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated).
- 3. Physical exam: Valsalva results, status of TM.
- 4. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 5. Audiogram. (If an audiogram profile is not H-1, a full audiology evaluation is needed).
- 6. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 7. Otolaryngology consultation; attach referral report.FL4 with RTD and ALC status, if member did not meet retention status
- 8. Copy of surgery report.
- 9. If the local base is not able to provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1 Assessment for recurrence (e.g., otorrhea, otalgia, hearing loss, etc.).
- 2 Physical exam: Valsalva results and status of TM.
- 3 Audiogram. (If an audiogram profile is not H-1, a full audiology evaluation is needed).
- 4 Otolaryngology consultation; attach referral report.
- If the local base is not able to provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Cholesteatomas are typically classified based upon their pathogenesis, being either acquired or congenital. Acquired cholesteatomas are the most common form of cholesteatoma found in the general population and in USAF aircrews. Acquired cholesteatomas may be further subdivided into primary or secondary. Primary acquired cholesteatomas, which account for up to 80% of all middle ear cholesteatomas, seem to occur behind an intact TM. Secondary acquired cholesteatomas, which account for 18% of middle ear cholesteatoma, seem to "grow" into the middle ear through a perforated TM. Congenital cholesteatomas are rare, and account for only about 2 to 4% of all middle ear cholesteatomas.

The pathogenesis of acquired cholesteatoma has been debated for over a century, but the most commonly agreed upon etiological factors include chronic eustachian tube dysfunction, poor pneumatization of the middle ear and mastoid process, and inflammatory conditions (e.g., chronic otitis media with effusion), and subsequent retraction pocket formation.

Aeromedical concerns regarding cholesteatomas include hearing loss, vertigo, facial paralysis, intracranial suppurations, recurrence, persistent eustachian tube dysfunction, and otalgia (aggravated with headset or helmet use). Improved surgical techniques have decreased morbidity and mortality from this disease, however, patient outcome depends on the extent of the disease at the time of surgery and the skill of the surgeon. Although many patients will have normal ear function for decades after surgical excision, cholesteatoma may recur and require multiple operations and may result in diminished hearing. In most patients, the underlying cause, e.g., eustachian tube dysfunction will persist.

A review of AIMWTS through Dec 2018 revealed a total of 54 cases with an AMS containing the diagnosis of cholesteatoma, 4 of these cases resulted in a disqualification disposition (all FC III). Breakdown of the cases revealed: 3 FC I/IA cases, 19 FC II/IIA cases, 27 FC III cases, 2 ATC/GBC cases, and 3 MOD cases.

| ICD-9 codes for cholesteatoma |   |  |
|-------------------------------|---|--|
| 385.3                         | Cholesteatoma of middle ear and mastoid |  |
| 385.30                        | Cholesteatoma, unspecified              |  |
| 385.31                        | Cholesteatoma of attic                  |  |
| 385.32                        | Cholesteatoma of middle ear             |  |
| 385.33                        | Cholesteatoma of middle ear and mastoid |  |
| 385.35                        | Diffuse cholesteatoma                   |  |
| 383.32                        | Recurrent postmastoidectomy cavity      |  |

| ICD-10 codes for cholesteatoma |   |  |
|--------------------------------|---|--|
| H71.9                          | Unspecified cholesteatoma, right, left,         |  |
| 0, 1, 2, 3                     | bilateral                                       |  |
| H71.0                          | Cholesteatoma of attic, unspecified ear, right, |  |
| 0, 1, 2, 3                     | left, bilateral                                 |  |
| H71.1                          | Cholesteatoma of tympanum, unspecified ear      |  |
| H71.2                          | Cholesteatoma of mastoid, unspecified ear,      |  |
| 0, 1, 2, 3                     | right, left, bilateral                          |  |
| H71.30                         | Diffuse cholesteatoma, unspecified ear          |  |
| H95.00                         | Recurrent cholesteatoma of                      |  |
|                                | postmastoidectomy cavity, unspecified ear       |  |

## **IV. Suggested Readings**

- 1. Basic Otorhinolaryngology: A Step-by-Step Learning Guide, 2nd Edition. (2018). *ProtoView*, 2018(9), ProtoView, Vol.2018(9).
- 2. Cholesteatoma. (2012). Reference *and Research Book News*, 27(1), Reference and Research Book News, Vol.27(1).
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### **Color Vision Deficiencies (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons, (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** None. Despite the change in Flying Class categories, the RPA, RPA SO standard remains at CCT-55 minimum, and the MOD remains at CCT-35. MSD C80.

#### I. Waiver Consideration

Moderate and Severe color vision deficiencies are disqualifying for FC I/IA, II, III, ATC, SWA, and GBO personnel. Severe color vision deficiency is disqualifying for MOD personnel. A normal score on the CCT is 75 or better. A score of 55 or better is required for FC I/IA, II, III, ATC, SWA, RPA and RPA SO duties and a score of 35 or better is required for MOD duties. Untrained aircrew will not be considered for waiver below the MSD standard. Trained aircrew may be considered for a waiver for defective color vision. ACS review/evaluation is required as part of the waiver consideration for trained aircrew. Waiver recommendations and management are primarily dependent on the etiology, severity of the color deficiency, and are made on a case by case basis. Indefinite waivers for color vision deficiency are authorized. CCT testing is required once at initial qualification. A CCT score of 55-74 is considered mild color deficiency; a score of 35-54 is moderate color deficiency, and a score < 35 is considered severe color deficiency.

Table 1: Waiver potential for Color Vision Deficiencies.

| Flying Class                 | Passing  | Waiver Potential   | ACS Review/Evaluation      |
|------------------------------|----------|--------------------|----------------------------|
|                              | Score    |                    |                            |
| FC I/IA,                     | CCT - 55 | No                 | No                         |
| Initial FC II/III, ATC, SWA, |          |                    |                            |
| GBO (RPA, RPA SO)            |          |                    |                            |
| Initial MOD                  | CCT - 35 | Maybe <sup>1</sup> | Yes                        |
| Trained FC II /III           | CCT - 55 | Yes                | Yes - At the discretion of |
| ATC, SWA, GBO (RPA,          |          | FCIIC <sup>2</sup> | MAJCOM.                    |
| RPA SO)                      |          |                    |                            |
| MOD                          | CCT - 35 | Yes <sup>1</sup>   | Yes - At the discretion of |
|                              |          |                    | AFMRA <sup>1</sup>         |

<sup>1</sup> MOD waivers are unlikely but will be considered on a case-by-case basis, with inputs from the career field manager and AFMRA if needed.

AIMWTS search in Jun 2018 revealed a total of 3467 individuals with an AMS containing a diagnosis of color deficiency. Of that total, 1536 were disqualified. Breakdown of the cases was as follows: 501 FC I/IA (476 DQ), 785 FC II (41 DQ), 52 RPA pilots (34 DQ),

<sup>2</sup> Flying Class IIC waiver restricted to all previously flown aircraft. If selected to cross train into a new airframe, or assigned to a previous airframe that has undergone a significant cockpit upgrade that requires interpretation of different color symbology, an operational evaluation is recommended to verify capability to accurately recognize and respond to all display information. This operational evaluation should be performed by an instructor pilot in the new airframe.

1509 FC III (592 DQ), 372 ATC/GBC (226 DQ), and 248 MOD (167 DQ). Within the DQ category, there were 13 ETP cases (3 FC I, 9 FC III, and 1 MOD). Of this total, 11 were denied and 2 were granted (both FC III).

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

## A. First-time (Indefinite) Waiver Request:

- 1. History history of previous color vision testing results (MEPS, commissioning, initial flying physicals, preventive health assessments), family history of color vision defects, medications, and any impact on job/daily life.
- 2. Physical Full eye exam to include funduscopic results and current color testing results on the most recent CCT version (ensure proper positioning and alignment with correction to at least 20/20 at distance and near or best corrected if member does not have 20/20 vision potential).
- 3. Optometry or ophthalmology consultation report.

### **III. Aeromedical Concerns**

Color deficient individuals are at a distinct disadvantage in terms of receiving and processing information in an efficient manner in the aviation and occupational environment. This can be demonstrated in aviation history as witnessed in the FedEx mishap in 2002, where color vision was found to be a contributing factor. Several other examples have been cited in a work on military aviation history and color vision. With regards to aviation, color defectives are more vulnerable to low-light and hypoxic effects on color vision than normals. Additionally, one must consider the compounding effects induced by certain required protective or performance enhancing optical appliances that can potentially degrade existing levels of color perception even further. These currently include blue-blocker sunglasses, yellow high-contrast visors, and assorted laser eye protection devices. While these devices cause changes in color perception with color normal subjects, the impact is far more profound with subjects who have an underlying color deficit. This finding is the basis for restriction from use of the yellow high contrast visor by color defective members, as stated in AFI 48-123. In addition to concerns with flying members, color vision can pose a significant risk for ground personnel. Color discrimination is an integral capability in the function of many ground based duties, to include remotely piloted aircraft operations and air-traffic control duties. Previous studies have demonstrated the importance of normal color vision in performing crucial tasks in air-traffic control. In light of changing technology both in operational symbology and color vision screening, the Operational Based Vision Assessment (OBVA) lab and ACS Ophthalmology are testing to determine if any updates on color vision requirements can be made for the various career fields. However, the current device being investigated by OBVA, the Konan CCT-HD, has not been validated for accuracy and consistency at scoring for a 55 cutoff and is not approved for initial flying class physical exam testing. Additionally, Innova is now selling tablets to various flight medicine clinics for color

vision testing to be held anywhere from 18-24 inches from the tester. As a result, there is a surge of applicants who are able to pass on the tablet at the local base by holding the screen closer (which makes the image larger), but ultimately fail at MFS when the approved NCI test at 36 inches and confirmatory ancillary testing are properly administered. Therefore, the Konan CCT-HD and the Innova are not approved or recommended for initial flying class physical exams.

In general, most color vision screening tests involve one of three types: pseudoisochromatic plates [or PIP (e.g. Ishihara)], an arrangement test (e.g. D-15 or FM-100), or an operationally derived test (e.g. FALANT). While these tests are appropriate for screening purposes, they are highly dependent on proper administration and they are not designed to quantify severity of color deficiencies. To address these concerns, USAF School of Aerospace Medicine scientists developed the computer-based Rabin Cone Contrast Test (CCT). A study with aircrew applicants demonstrated that the CCT significantly improves sensitivity relative to pseudo-isochromatic plates and provides quantification on the level of color deficiency. Due to these advances, the CCT is now the only acceptable device for evaluating color vision of USAF aircrew and applicants to aircrew positions. A normal score on the CCT is 75 or better. A passing score on the CCT is now 55 or greater (mild deficiency or better) for the red, green, and blue cone types with each eye (35 or better is required for MOD duties). To ensure the most accurate results, testing should be accomplished with the patient corrected to 20/20 at distance and near or best corrected if member does not have 20/20 vision potential. It is appropriate to use a reading lens for the test distance (36 inches) for presbyopic patients as needed. Alignment of the monitor should be confirmed using the alignment tube and the patient should not be allowed to move their head during the test sequence (refer to the KX for further guidance). Improper test administration can result in false positive and false negative results.

| ICD-9 codes for color vision deficiency |  |  |
|---|--|--|
| 368.51                                  | Protan defect                          |  |
| 368.52                                  | Deutan defect                          |  |
| 368.59                                  | Color vision deficiencies, unspecified |  |

| ICD-10 codes for color vision deficiency |                                       |  |
|--|---------------------------------------|--|
| H53.54                                   | Protanomaly                           |  |
| H53.53                                   | Deuteranomaly                         |  |
| H53.50                                   | Unspecified color vision deficiencies |  |
| H53.59                                   | Other color vision deficiencies       |  |

## **IV. Suggested Readings**

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### WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of May 2013

By: Dr. Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for oncology, Lt Col Thomas Stamp, AF/SG consultant for general surgery, and Lt Col Eric Plott, AF/SG consultant for gastroenterology, and AFMSA staff.

### **CONDITION:**

Colorectal Cancer (Jan 2018)

### I. Waiver Considerations.

CRC, or a history of CRC, is disqualifying for all classes of flying and special duties in the US Air Force. It is not listed specifically as disqualifying however MSD O1 applies: "Malignant Neoplasms. All malignant neoplasms (except basal cell or squamous cell carcinomas of the skin, and cervical carcinomas-in-situ, after surgical cure) require I-RILO processing." There are no indefinite waivers for this condition.

Table 1: Waiver potential of colorectal cancer in FC I/IA, II and III

| Flying Class | Condition         | Waiver Potential | ACS review/evaluation |
|--------------|-------------------|------------------|-----------------------|
| (FC)         |                   | Waiver Authority |                       |
| I/IA         | Stages I or II    | Yes#             | Yes                   |
|              |                   | AETC             |                       |
|              |                   |                  |                       |
|              | Stage IIIA, B, or | No               | No                    |
|              | C                 | AETC             |                       |
|              |                   |                  |                       |
|              |                   | No               | No                    |
|              | Stage IV          | AETC             |                       |
| II/III       | Stages I or II    | Yes+*            | Yes                   |
| ATC/GBO/SWA  |                   | AFMRA            |                       |
|              |                   |                  |                       |
|              | Stage IIIA, B, or | Maybe+*          | Yes                   |
|              | C                 | AFMRA            |                       |
|              |                   |                  |                       |
|              |                   | No               | No                    |
|              | Stage IV          | AFMRA            |                       |

<sup>#</sup> For FC I/IA individuals, waiver may be considered after five years of remission, asymptomatic.

AIMWTS review in Jan 2018 revealed a total of 47 submitted cases of CRC. Breakdown of the cases was as follows: one FC I case (disqualified), 26 FC II cases (5 disqualified), 18 FC III cases (4 disqualified), 2 MOD cases (1 disqualified), and 0 ATC/GBC cases. Of

<sup>+</sup> For trained personnel waiver may be considered as early as six months after treatment completed, in remission, surveillance is ongoing, and asymptomatic.

<sup>\*</sup> For untrained personnel, waiver may be considered after five years of remission.

the 11 disqualified cases, 7 were disqualified due to advanced disease, 2 for multiple medical problems and the FC I case because it was too soon to consider.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for initial waiver for CRC should include the following:

- A. History initial symptoms, colonoscopy (or CTC) findings, pathology, stage, treatment, surveillance plan, and activity level.
- B. Physical abdominal, rectal, and all imaging studies.
- C. GI and surgeon reports to include all follow-up studies, to include a clean colonoscopy..
- D. Labs Serial CBCs and carcinoembryonic-antigen test results; must be normal to be considered for a waiver.
- E. Tumor board report, military or civilian, if applicable.
- F. Medical evaluation board results.

The AMS of <u>waiver renewal</u> of CRC should include the following:

- A. History brief summary of stage, treatment, frequency of surveillance and results, any symptoms, activity level.
- B. Physical abdominal and rectal exams and imaging studies, if done.
- C. Oncology consult(s).
- D. Labs all CBCs and carcinoembryonic-antigen test results since previous waiver.
- E. Evidence that the level of follow-up care is consistent with current NCCN standards.

#### III. Overview.

Colorectal cancer (CRC) is the fourth most common cancer in the US and is the second leading cause of cancer-related mortality. In 2016 an estimated 135,000 new cases of colorectal cancer were responsible for an estimated 49,000 CRC related deaths. <sup>1, 2, 3</sup> CRC is the third leading cause of cancer deaths in both men and woman. Prior to age 50, men and woman have essentially equal incidence and mortality rates. After age 50, the rates are higher in men. Racial and ethnic groups have differing incidence and mortality rates. African Americans have the highest rates while Hispanics and Pacific Islanders have the lowest. <sup>4</sup> The overall 5-year survival in the US continues to improve mostly from increased utilization of screening tests. <sup>4, 5</sup> Unfortunately, the incidence of CRC in persons younger than 50 years of age has been increasing. With current trends, estimates for the 20-34 year old age group are for more than a 120% increase in CRC incidence by 2030. <sup>1</sup> The disease is often insidious in development and common symptoms are fatigue, anemia, altered bowel function, pain and weight loss. The most common acute surgical problem is bowel obstruction.

CRC has been linked to both genetic and environmental factors. Those genetic factors that influence screening recommendations include: hereditary colorectal cancer syndromes such as familial adenomatous polyposis, MUTYH-associated polyposis, and Lynch syndrome, as well as family or personal history of sporadic colorectal cancer. Although inherited susceptibility results in the most striking increases in risk, the majority of CRCs are sporadic rather than familial, with the hereditary syndromes accounting for less than 10% of cases.<sup>6,7</sup>

Most CRCs are adenocarcinomas and arise from existing adenomatous polyps. In addition to familial risk, inflammatory bowel disease (ulcerative colitis and Crohn's Disease) is a well-established risk factor for development of CRC. As well, increasing age and male gender are associated with increased risk. Other risk factors include alcohol use and increased body mass index. There is ongoing research concerning evidence that supports the role of abdominal radiation, acromegaly, renal transplantation, diabetes mellitus and cholecystectomy to an individual's risk of disease. Substantial data exists that a lifestyle with regular exercise, and containing a diet that is high in fruits and vegetables, can lower ones risk for colorectal cancer. More research is necessary before conclusions can be made on calcium, vitamin B6, folic acid, fiber, and fish consumption.

Current screening recommendations are for all Americans to have an initial screening starting at age 50 (45 for African Americans). Options for screening from the US Multisociety Task Force on Colorectal Cancer include: (1) annual fecal occult blood test, (2) flexible sigmoidoscopy every five years, (3) combination of (1) and (2) above, (4) colonoscopy every ten years, and (5) CT colonography every five years. This has led to the reduced mortality for CRC seen in most US populations. The initial screening colonoscopy should be performed at an earlier age for individuals with genetic, familial, and other risk factors. Surveillance colonoscopy should be performed at increased intervals in individuals with certain pathologic findings on index screening exam. 9, 10

Colonic adenomas are the precursors to almost all CRCs and are found in up to 40% of all persons by the age of 60. As most colonic polyps are adenomas and more than 90% of adenomas probably do not progress to CRC, it is not currently possible to reliably identify those polyps that will progress. Larger polyp size and more advanced histologic features are more predictive of progression to invasive cancer. Identification and removal of these "pre-cancerous" lesions is the primary purpose of screening colonoscopy and mode by which this procedure can reduce incidence of CRC.

Surgery is the cornerstone of therapy for CRC and 70 to 80 percent of patients with tumors can be resected with curative intent. Among patients who have undergone resection for localized disease, the five-year survival rate is 90%. The survival rate decreases to 65% when metastasis to regional lymph nodes is present. Most recurrences occur within three years, and 90% occurs within five years. The most common sites of recurrence are the liver, the local site, the abdomen and the lung. Prospective studies have demonstrated that the use of chemotherapy in patients with metastatic disease prolongs survival and enhances quality of life in comparison to palliative care alone. Adjuvant radiation therapy is frequently used for treatment of rectal cancer.

There has been much debate over the years on how best to follow patients post-treatment for CRC. After it has been concluded that the colon is free of cancer and polyps, colonoscopy is recommended at one, three, and every five years thereafter, depending on patient characteristics. Physician visits with targeted exams are recommended every 3 to 6 months for the first three years with decreased frequency thereafter for 2 additional years. There is also consensus that patients be tested every 3 to 6 months for up to 5 years with a carcinoembryonic-antigen test, as most recurrences will first be detected with this lab.<sup>14</sup>

While in-depth diagnostic, staging, and treatment regimens associated with CRC are beyond the scope of this document, a staging overview is included below for reference. As well, a succinct presentation of guidelines related to colorectal cancer, screening modalities and specifics, hereditary syndromes, etc. is published by the National Comprehensive Cancer Network and available at https://www.nccn.org.

## Staging of Colorectal Cancer

**Table 2. American Joint Committee on Cancer (AJCC) Colon Cancer Staging System** 

| Stage (T) | Primary Tumor (T)  |
|-----------|--|
| TX        | Primary Tumor cannot be assessed                                     |
| <b>T0</b> | No evidence of primary tumor   |
| Tis       | Carcinoma in situ: intraepithelial or invasion of lamina propria     |
| <b>T1</b> | Tumor invades submucosa  |
| <b>T2</b> | Tumor invades muscularis propria                                     |
| <b>T3</b> | Tumor invades through the muscularis propria into the subserosa, or  |
|           | into non-peritonealized pericolic or perirectal tissues              |
| <b>T4</b> | Tumor directly invades other organs or structures, and/or perforates |
|           | visceral peritoneum  |
|           |  |
|           | Regional Lymph Nodes   |
| NX        | Regional lymph nodes not assessed                                    |
| N0        | No regional lymph node metastasis                                    |
| N1        | Metastasis in 1 to 3 regional lymph nodes                            |
| N2        | Metastasis in 4 or more regional lymph nodes                         |
|           |  |
|           | Distant Metastasis   |
| MX        | Distant metastasis cannot be assessed                                |
| M0        | No distant metastasis  |
| M1        | Distant metastasis   |

**Table 3 Stage Grouping for Colorectal Cancer** 

| Stage | Primary   | Regional  | Distant      | Dukes | MAC      |
|-------|-----------|-----------|--------------|-------|----------|
|       | Tumor (T) | Lymph     | Metastasis   |       |          |
|       |           | Nodes (N) | ( <b>M</b> ) |       |          |
| 0     | Tis       | N0        | M0           | -     | _        |
| I     | T1        | N0        | M0           | A     | A        |
|       | T2        | N0        | M0           | A     | B1       |
| IIA   | T3        | N0        | M0           | В     | B2       |
| IIB   | T4        | N0        | M0           | В     | B3       |
| IIIA  | T1-T2     | N1        | M0           | C     | C1       |
| IIIB  | T3-T4     | N1        | M0           | C     | C2/C3    |
| IIIC  | Any T     | N2        | M0           | C     | C1/C2/C3 |
| IV    | Any T     | Any N     | M1           | -     | D        |

#### IV. Aeromedical Concerns.

Of significant concern with CRC is the potential for sudden incapacitation as the initial presentation; emergent obstruction, or perforation. Chronic anemia presents more insidiously and can cause in-flight problems if undetected. CRC has primarily affected persons over 50 years of age, thereby removing a majority of USAF aviators from the high risk window. As mentioned previously, however, the incidence CRC in the 20-34 age group is on the rise, potentially recapturing those aviators into this risk pool. Regular screening may decrease late presentations and any alarm features, even at a young age, should be carefully considered.

Once diagnosed and treated, the potential for recurrence becomes an important health and aeromedical concern. It has been shown that 80 to 90 percent of all recurrences following curative resection occur within the first 2-3 years and that 95% occur within five years. The five-year survival point can be used as a reliable mark of cure. Among those who undergo curative resection, colonic reanastomosis is common. The presence of colostomy or ileostomy, however, is not compatible with military aviation (MSD I40).

| ICD9 Codes | ICD9 Codes for Colorectal Cancer                                      |  |  |
|------------|---|--|--|
| 153.0      | Malignant neoplasm of hepatic flexure                                 |  |  |
| 153.1      | Malignant neoplasm of transverse colon                                |  |  |
| 153.2      | Malignant neoplasm of descending colon                                |  |  |
| 153.4      | Malignant neoplasm of cecum   |  |  |
| 153.6      | Malignant neoplasm of ascending colon                                 |  |  |
| 153.7      | Malignant neoplasm of splenic flexure                                 |  |  |
| 153.8      | Malignant neoplasm of other specified sites of large intestine        |  |  |
| 153.9      | Malignant neoplasm of colon, unspecified                              |  |  |
| 154.0      | Malignant neoplasm of rectosigmoid junction                           |  |  |
| 154.1      | Malignant neoplasm of rectum  |  |  |
| 154.8      | Malignant neoplasm of other sites of rectum, rectosigmoid junction, & |  |  |
|            | anus  |  |  |

| ICD-10 Cod | es for Colorectal Cancer  |
|------------|---|
| C18.3      | Malignant neoplasm of hepatic flexure                                 |
| C18.4      | Malignant neoplasm of transverse colon                                |
| C7A.023    | Malignant carcinoid tumor of the transverse colon                     |
| C18.6      | Malignant neoplasm of descending colon                                |
| C7A.024    | Malignant carcinoid tumor of the descending colon                     |
| C18.0      | Malignant neoplasm of cecum   |
| C7A.021    | Malignant carcinoid tumor of the cecum                                |
| C18.2      | Malignant neoplasm of ascending colon                                 |
| C7A.022    | Malignant carcinoid tumor of the ascending colon                      |
| C18.5      | Malignant neoplasm of splenic flexure                                 |
| C18.9      | Malignant neoplasm of colon, unspecified                              |
| C7A.029    | Malignant carcinoid tumor of the large intestine, unspecified portion |
| C18.7      | Malignant neoplasm of sigmoid colon                                   |
| C7A.025    | Malignant carcinoid tumor of the sigmoid colon                        |
| C20        | Malignant neoplasm of rectum  |
| C7A.026    | Malignant carcinoid tumor of the rectum                               |
| C18.8      | Malignant neoplasm of overlapping sites of the colon                  |

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#### WAIVER GUIDE

Updated: Feb 2015

Supersedes Waiver Guide of Sep 2011

By: Dr Dan Van Syoc, Lt Col Steven Gore and Maj Eddie Davenport (ACS chief

cardiologist),

### **CONDITION:**

**Congenital Heart Disease (Feb 2015)** 

### I. Waiver Consideration.

Congenital heart defects, uncorrected or corrected by surgical or catheter-based procedures, are disqualifying for flying class (FC) I/IA, II, and III. Congenital and structural anomalies of the heart that are not normal structural variants, other than PFO are not qualified for retention, so ATC, SWA, and GBO personnel would need a waiver, as they require an MEB. In addition, any history of cardiac surgery or catheter-based therapeutic intervention (including closure of PFO) is disqualifying for all flying classes. ASD, VSD and PDA successfully corrected by surgery or catheter-based techniques, especially in childhood, may be favorably considered for waiver for all classes of flying duties, as may uncorrected, but hemodynamically insignificant ASD and VSD. Because the appropriate treatment of hemodynamically insignificant PDA is unsettled, uncorrected small PDAs will be considered on a case-by-case basis. Coarctation of the aorta will also be considered on a case-by-case basis.

Table 1: Waiver potential for congenital heart defects\*\*

|                                | Table 1: Waiver potential for congenital heart defects** |                   |                   |  |  |
|--------------------------------|--|-------------------|-------------------|--|--|
| Flying Class                   | Condition  | Waiver            | ACS               |  |  |
|                                |  | Potential         | Review/Evaluation |  |  |
|                                |  | Waiver            |                   |  |  |
|                                |  | Authority         |                   |  |  |
| I/IA                           | Hemodynamically insignificant ASD, VSD, PDA              | Yes<br>AETC       | Yes               |  |  |
|                                | Hemodynamically significant ASD, VSD, PDA (uncorrected)  | No<br>AETC        | No                |  |  |
|                                | Hemodynamically significant ASD, VSD, PDA (corrected)    | Yes#<br>AETC      | Yes               |  |  |
|                                | Coarctation of aorta                                     | Maybe*#<br>AETC   | Yes               |  |  |
|                                | PFO surgically closed                                    | Maybe<br>AETC     | Yes               |  |  |
|                                | PFO asymptomatic/incidental finding                      | N/A (not DQ)      | No                |  |  |
| II/III and initial GBO/ATC/SWA | Hemodynamically insignificant ASD, VSD, PDA              | Yes<br>MAJCOM     | Yes               |  |  |
|                                | Hemodynamically significant ASD, VSD, PDA (uncorrected)  | No<br>MAJCOM      | No                |  |  |
|                                | Hemodynamically significant ASD, VSD, PDA (corrected)    | Yes#<br>MAJCOM    | Yes               |  |  |
|                                | Coarctation of aorta                                     | Maybe#<br>MAJCOM  | Yes               |  |  |
|                                | PFO surgically closed                                    | Maybe*#<br>MAJCOM | Yes               |  |  |
|                                | PFO asymptomatic/incidental finding                      | N/A (Not DQ)      | No                |  |  |
| ATC/GBO/SWA                    | Any congenital heart defect                              | Maybe<br>MAJCOM   | No                |  |  |

<sup>#</sup> Must wait at least six months after surgery before submitting waiver.

AIMWTS search in Feb 2015 revealed 96 aeromedical summaries with a diagnosis of ASD, VSD, PFO, PDA, or coarctation. Breakdown of the cases revealed: 12 FC I/IA cases (2 disqualified), 32 FC II cases (4 disqualified), 45 FC III cases (12 disqualified), 3

<sup>\*</sup> Not waiverable if PFO closed due to TIA or CVA episode. See TIA/CVA Waiver Guide.

<sup>\*\*</sup> Per AFI 48-123 6.4.1.3, AFMRA remains waiver authority for all initial waivers for conditions that do not meet retention standards, unless 6.4.1.4.1 applies.

ATC/GBC cases (no disqualifications), and 4 MOD cases (1 disqualified). Only 5 of the 19 disqualified cases were disqualified specifically for the congenital abnormality.

### II. Information Required for Waiver Submission.

The aeromedical summary should only be submitted after administrative and clinical disposition have been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for initial waiver should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, treatment, medications, and activity level.
- B. Cardiology consultation.
- C. Electrocardiogram (ECG).
- D. Official report of all local echocardiograms. Also send videotape/CD copy of the images of the most recent echocardiogram to the ACS [if recent surgery, echocardiogram should be done close to six months after surgery]. (Notes 1 and 2)
- E. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- F. Operative report, if recent surgery.
- G. Results of medical evaluation board (MEB) (worldwide duty evaluation for ARC members), if congenital abnormalities not satisfactorily treated by surgical correction.

The aeromedical summary for <u>waiver renewal</u> should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, treatment, medications, and activity level.
- B. Electrocardiogram (ECG).
- C. Additional local cardiac testing is not routinely required for re-evaluation cases followed at the ACS but may be requested in individual cases. If so, the previous ACS evaluation/review will specify details regarding any requested local testing.
- D. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI

Facility 20840 2510 Fifth Street

WPAFB, OH 45433-7913

Note 2: State in AMS when studies were sent to ACS.

### III. Overview.

Congenital heart disease (CHD) is estimated to involve up to 1% of live births in the US.<sup>1,2</sup> CHD in adults includes common and uncommon defects, with and without correction by surgery or catheter-based interventions. Consideration of waiver for continued military flying duties or training require normal or near-normal cardiovascular status, acceptably low risk of aeromedically pertinent events, and no significant residua. Since the advent of reparative surgery for congenital cardiac defects, it is estimated that 85% of affected children survive into adulthood.<sup>3</sup> In 2010, researchers estimated there are approximately 1.1 million Americans over the age of 18 with congenital heart disease.<sup>12</sup> Longitudinal studies estimate that approximately 20% of individuals with CHD will experience tachyarrhythmias during their lifetime which can possibly become an aeromedical concern.<sup>2</sup>

Bicuspid aortic valve is discussed in the Bicuspid Aortic Valve Waiver Guide. Otherwise, the most common congenital disorders that will require aeromedical consideration are the atrial septal defect (ASD), ventricular septal defect (VSD), and patent foramen ovale (PFO) with/without associated atrial septal aneurysm (ASA). Patent ductus arteriosus (PDA) and coarctation of the aorta may also be seen. Hemodynamically significant defects are likely to be detected and corrected during infancy or childhood, especially VSD and PDA. Other, more complicated congenital disorders will be very unusual because most will be detected in infancy or childhood and, even if corrected, will be unacceptable for entrance into military service.

## ATRIAL SEPTAL DEFECT (ASD)

There are three types of ASD; ostium secundum (75%) [failure of the septum primum to cover the fossa ovalis], ostium primum (15%) [inadequate development of the endocardial cushion, thus failing to close the ostium primum], and sinus venous (10%) [abnormal embryologic evolution of the sinus venous and sinus valves]. ASDs allow shunting of blood flow from the left to right atrium, with resultant right-sided volume overload and enlargement of the right atrium and ventricle. Presence and time course of symptom development depends on the magnitude of the shunt with shunts greater than a 1.5 pulmonary to systemic flow ratio (Qp:Qs) generally producing significant volume overload with resultant symptoms, including easy fatigue, dyspnea, and arrhythmias, especially atrial fibrillation. Straining, coughing, Valsalva, anti-G straining maneuvers or positive pressure breathing may cause the blood flow to reverse, which could serve as conduit for embolic material. Moderate and even large sized ASDs may not be detected until adulthood. Many patients are minimally symptomatic during the first three decades of life although more that 70% became somewhat impaired by the fifth decade.<sup>4</sup> Prognosis after successful and uncomplicated closure of significant secundum and sinus venosus ASD is normal if accomplished before age 25.5-7 Closure later in life increases the risk of atrial fibrillation, stroke, and right heart failure.

### VENTRICULAR SEPTAL DEFECT (VSD)

Hemodynamically significant defects are likely to be detected and corrected during infancy or childhood. Hemodynamically insignificant VSDs will also likely be detected in

infancy or childhood due to the very characteristic murmur but may not be recommended for closure because of insignificant shunting and a high likelihood of spontaneous closure over time. VSDs repaired before age 2 have a good long-term prognosis.<sup>7</sup>

## PATENT DUCTUS ARTERIOSUS (PDA)

PDAs classically produce a prominent continuous "machinery" murmur heard at the second left intercostal space. Small PDAs may escape detection until adolescence or adulthood but are unusual. In the past, even small PDAs were often recommended for surgical or catheter-based closure due to anticipated long-term risks of heart failure, endocarditis and pulmonary hypertension. Recently, a trend has developed to follow small PDAs, especially silent PDAs, without correction/closure. The proper course of therapy for small PDAs is not yet established and there is disagreement among experts as to the theoretical increased risk of endocarditis in small and silent PDAs.

### COARCTATION OF THE AORTA

Coarctation of the aorta results in elevated blood pressure in the upper limbs, with normal or low pressure in the lower limbs. Associated abnormalities with coarctation include bicuspid aortic valve, congenital aneurysms of the circle of Willis, and aortic aneurysms. Unrepaired coarctation with a resting gradient  $\geq 20$  mm Hg between the upper and lower extremities carries an increased risk for progressive left ventricular hypertrophy and subsequent left ventricular dysfunction, persistent systolic hypertension, and premature atherosclerotic cerebrovascular and coronary heart disease. Coarctation of the aorta is usually diagnosed in childhood, but up to 20% of cases are reportedly not detected until adolescence or adulthood. Long-term prognosis is related to the age of repair, with the best outcome for correction being before age 9.8

## PATENT FORAMEN OVALE (PFO) and ATRIAL SEPTAL ANEURYSM (ASA)

Patent foramen ovale (PFO) and atrial septal aneurysm (ASA) are anatomic anomalies of the interatrial septum. PFO occurs in 25-30% of the general population. At that prevalence, it can be considered a normal variant. ASA is present in about 1-2% of the general population. PFO and ASA may be present alone or may occur together. Asymptomatic PFO and/or ASA are typically incidental findings discovered on echocardiogram evaluation performed for unrelated indications. Aeromedically, these are considered normal anatomic variants and therefore are qualifying for all classes of flying duties including initial training.

Despite these defects being considered normal anatomic variants for aeromedical evaluation, PFO and ASA, alone or in combination, have been associated with possible paradoxical embolic events, notably stroke and transient ischemic attack. Although the relative risk for such an event may be increased, the absolute risk is low. The 2010 published CLOSURE trial showed no decrease in recurrent stroke after PFO closure (via percutaneous device) and a possibly significant vascular complication rate and increased risk of atrial fibrillation after PFO closure. Additionally, there was still a 3.1% stroke rate in both the medical and PFO closure arms of the trial. More recently, the 2013 published PC and RESPECT trials both found that device closure of a PFO did not offer a significant benefit over medical therapy for the prevention of recurrent ischemic stroke. Although the relative risk is low. The 2010 published PC and RESPECT trials both found that device closure of a PFO did not offer a significant benefit over medical therapy for the prevention of recurrent ischemic stroke.

<sup>15</sup> Therefore, asymptomatic and hemodynamically insignificant PFO by itself is considered a normal variant and does not require waiver UNLESS it has been surgically (to include percutaneously) closed. TIA/CVA is not usually waiverable. Aeromedical concerns and recommendations for PFO and/or ASA associated with stroke or transient ischemic attacks are also discussed in the Transient Ischemic Attack (TIA) and Stroke (CVA) Waiver Guide. All aeromedical instructions in this waiver guide regarding PFO associated with CVA/TIA apply equally to ASA associated with CVA/TIA.

#### II. Aeromedical Concerns.

Aeromedical concerns for all congenital heart disease are primarily related to the long-term effects of shunting with volume overload. These include atrial and ventricular dilation and dysfunction, tachydysrhythmias, endocarditis or endarteritis. For those treated surgically, favorable results need to be well demonstrated.

| ICD-9 Codes for congenital heart diseases |   |  |
|---|---|--|
| 745.4                                     | Ventricular septal defect                                     |  |
| 745.5                                     | Patent foramen ovale and ostium secundum atrial septal defect |  |
| 745.6                                     | Ostium primum atrial septal defect                            |  |
| 745.9                                     | Unspecified defect of septal closure                          |  |
| 747.0                                     | Patent ductus arteriosus                                      |  |
| 747.1                                     | Coarctation of aorta  |  |

| ICD-10 Codes for congenital heart diseases |   |  |
|--|---|--|
| Q21.0                                      | Ventricular septal defect   |  |
| Q21.1                                      | Atrial septal defect, patent foramen ovale, ostium primum atrial septal |  |
|  | defect, and ostium secundum atrial septal defect                        |  |
| Q21.9                                      | Congenital malformation of the cardiac septum, unspecified              |  |
| Q25.0                                      | Patent ductus arteriosus  |  |
| Q25.1                                      | Coarctation of aorta  |  |

#### V. References.

- 1. Dolbec K and Mick NW. Congenital Heart Disease. Emerg Med Clin N Am, 2011; 29: 811-27.
- 2. Asirvatham S, Connolly HM, and McLeod CJ. Atrial arrhythmias (including AV block) in congenital heart disease. UpToDate. Apr 2013.
- 3. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease. J Am Coll Cardiol, 2008; 52: e143-263.
- 4. Marelli AJ. Congenital Heart Disease in Adults. Ch. 69 in *Goldman's Cecil's Medicine*, 24<sup>th</sup> ed., Saunders, 2011.

- 5. Kruyer WB and Davenport ED. Cardiology. In: *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., New York: Castle Connolly Graduate Medical Publishing, LTD, 2013; 106-15.
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- 9. Furlan AJ, Reisman M, Massaro J, et al. A Prospective Multicenter, Randomized Controlled Trial to Evaluate the Safety and Efficacy of the STARflex Septal Closure System Versus Best Medical Therapy in Patients With a Stroke or Transient Ischemic Attack Due to Presumed Paradoxical Embolism Through a Patent Foramen Ovale. Stroke, 2010; 41: 2872-83.
- 10. Furlan AJ, Reisman M, Massaro J, et al. Closure or Medical Therapy for Cryptogenic Stroke with Patent Foramen Ovale. NEJM, 2012; 366: 991-99.
- 11. Johnston SC. Patent Foramen Ovale Closure Closing the Door Except for Trials. NEJM, 2012; 366: 1048-50.
- 12. Marelli A, Gilboa S, Owen, D, et al. Estimating the Congenital Heart Disease Population in the United States in 2010 What are the Numbers? J Am Coll Cardiol, 2012; 59(13s1): E787-E787.
- 13. Doyle DT, Kavanaugh-McHugh A, Soslow J, and Hill K. Management of patent ductus arteriosus. UpToDate. Feb 2014.
- 14. Meier B, Kalesan B, Mattle HP, et al. Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism. N Engl J Med, 2013; 368: 1083-91.
- 15. Carroll JD, Saver JL, Thaler DE, et al. Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke. N Eng J Med, 2013; 368: 1092-1100.

## **Congenital Urinary Anomalies (Jul 2019)**

Reviewed: Lt Col David Navel (RAM 20), Dr. Dan Van Syoc (ACS Waive Guide coordinator, Lt Col Christopher Allam (AF/SG urology consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Updated ICD-10 codes to include Q60.2, unspecified renal agenesis. Updated the new Waiver Guide format. Updated suggested readings.

#### I. Waiver Consideration

The following congenital urinary anomalies do not meet retention standards: any congenital urinary anomaly causing frequent absences from duty, polycystic kidney with abnormal renal function, or hypoplasia or other congenital or acquired abnormalities of the kidney that result in elevated blood pressure, frequent infections, or reduction in renal function. Any of these above conditions requiring specialty care more than annually is also disqualifying.

Congenital disorders of the urinary tract or genitalia of sufficient severity to cause distracting symptoms, frequent infections, or interfere with normal functioning do not require I-RILO but are disqualifying for all flying classes other than ATC, GBO, and Operational Support. Polycystic kidney with normal renal function, absence of a kidney, or a horseshoe kidney are disqualifying for FCI/IA, FCII/III, and SWA. Hydronephrosis, pyonephrosis, renal ptosis with impaired renal drainage or hypertension or pain, and functional impairment of either kidney are disqualifying for FCI/IA, FCII/III, SWA, ATC and GBO personnel.

After careful evaluation, most of these conditions can be considered for a waiver and will depend on the status of the underlying disease.

**Table 1: Waiver potential for Disease/Condition** 

| Flying Class (FC) | Disease/Condition <sup>1</sup>  | Waiver<br>Authority<br>Waiver<br>Potential | ACS<br>Review/<br>Evaluation |
|-------------------|---|--|------------------------------|
| FC I/IA           | PCKD <sup>2</sup> , absence of a kidney, horseshoe kidney, congenital disorders of the urinary tract, hydronephrosis, renal ptosis <sup>3</sup> | AETC<br>Yes <sup>4</sup>                   | Maybe                        |
| FC II/III/SWA     | PCKD <sup>2</sup> , absence of a kidney, horseshoe kidney, congenital disorders of the urinary tract, hydronephrosis, renal ptosis <sup>3</sup> | MAJCOM<br>Yes <sup>4</sup>                 | Maybe                        |
| ATC, GBO,<br>SWA  | Congenital disorders of the urinary tract, hydronephrosis, renal ptosis <sup>3</sup>  | MAJCOM<br>Yes <sup>4</sup>                 | No                           |

<sup>&</sup>lt;sup>1</sup>See above for stipulations of anomalies that do not meet retention standards

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated). Laboratory studies at a minimum should include a urinalysis, BUN and creatinine. The AMS should include a careful assessment of renal function and mention of presence or absence of stone disease.
- 3. Urology and/or Nephrology consultation reports, including follow-up notes with examination findings after disease resolution.
- 4. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 5. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 6. Current physical examination findings, including a GU exam and any pertinent imaging
- 7. FL4 with RTD and ALC status, if member did not meet retention status
- 8. If any of the above information cannot be provided, document why not to provide an explanation to the waiver authority

<sup>&</sup>lt;sup>2</sup>PCKD with normal renal function

<sup>&</sup>lt;sup>3</sup>Renal ptosis with impaired renal drainage, hypertension, or pain.

<sup>&</sup>lt;sup>4</sup>Waiver for initial certification needs to be considered very carefully. If the condition has a very low probability of leading to stone disease or decreasing renal function, then the candidate can be considered for a waiver.

## B. Renewal Waiver Request:

- Interim history to include change in symptoms (particularly renal function), medication usage, and side effects.
- 2 Exam: GU exam and result of all imaging tests.
- 3 Current treatment doses and documentation of therapeutic benefit.
- 4 Report from treating physician.
- 5 If any of the above information cannot be provided, document why not to provide an explanation to the waiver authority

### **III. Aeromedical Concerns**

Depending on the underlying condition, a number of symptoms may occur which could impair flying performance and mission completion. These include flank pain, renal stones, urinary urgency, urinary frequency, urinary obstruction, and dysuria all of which have the potential of sudden incapacitation. Recurrent infections and ongoing renal damage may lead to cortical scarring, hypertension, and compromised renal function. With these and other complications, close subspecialty follow-up incompatible with worldwide flying duties may be required.

While many or most presentations of these anomalies are asymptomatic, some have distinct features that warrant attention. Medullary sponge kidney (MSK) can present with renal colic, urinary tract infections, or hematuria. It is commonly found in patients with kidney stones and approximately 70% of patients with medullary sponge kidney will develop stones at some point. MSK itself is largely a benign process otherwise with little aeromedical impact. Horseshoe kidney is associated with hydronephrosis in about 80% of patients, kidney stones in 20%, and other genitourinary anomalies in about one-third. There is also an increased risk of urinary tract infection with horseshoe kidney. This condition itself poses minimal risk in flight provided the member does not have obstruction or stones. Polycystic kidney disease (PCKD) is associated an increased risk of kidney stones, anemia, urinary tract infections and hypertension. It is typically diagnosed during age 30-50 with presenting symptoms of hematuria (50%), renal colic and gastrointestinal symptoms. Elevated blood pressure or a decline in renal function indicates disease progression. Flank pain from enlarged kidneys or ruptured cysts can be significant. PCKD is associated with other abnormalities including liver cysts, cerebral aneurysms, pancreatic cysts, and cardiac valvular abnormalities that may affect flying. Close attention should be paid in PCKD patients to renal function, blood pressure, and a history of flank pain, all of which can have significant bearing in flight. A significant amount of PCKD patients can develop renal failure necessitating dialysis. Unilateral renal agenesis may be complicated by other genitourinary malformations and is associated with vesicoureteral reflux, increasing the risk of significant urinary tract infections. If the remaining kidney is functioning normally, there is usually little risk to flying. Congenital obstructions of the ureteropelvic junction (UPJ obstruction) often present with intermittent flank pain especially when the person is well-hydrated (Dietl's crisis). Obstructions can also present with abdominal pain, nausea and vomiting, worsening renal function or hematuria. Obstructions are associated with other anomalies listed above, particularly horseshoe kidney. A review of recently submitted waivers for frank obstruction revealed

that all members had the condition surgically or procedurally corrected and were therefore no longer symptomatic. This statistic may not be interpreted as law given that these members also presented with significant symptoms from their obstruction. Asymptomatic individuals or those with minimal symptoms may not pose a risk to flying. Renal ptosis, also known as floating kidney or nephroptosis, is characterized by a kidney that changes in position by more than 2 vertebral bodies between lying down and sitting up. Commonly asymptomatic, the positional movement of the kidney can cause vomiting or abdominal pain from obstruction or ischemia. Severe flank pain (Dietl's crisis) with sitting up in a thin female member that resolves upon lying down should warrant suspicion. Many patients will also have fibromuscular dysplasia of the renal artery leading to concurrent problems with hypertension. Nephropexy, or surgical fixation of the kidney, normally resolves symptomatic cases. Given the seated position of most aircrew, symptomatic nephroptosis is not normally compatible with flight. Renal ectopy occurs when one or both kidneys do not ascend to the retroperitoneal fossa, even sometimes failing to ascend out of the pelvis itself. Unilateral renal ectopy is often asymptomatic and would not pose a risk to aviation itself. Symptomatic renal ectopy can present with obstruction and recurrent urinary tract infections, particularly if associated with vesicoureteral reflux. It may also present as urinary incontinence due to pressure from safety restraints on the lower abdomen. These sequelae, along with a potential decline in renal function, can have an impact on flight.

Some of these conditions, such as medullary sponge kidney and horseshoe kidney, are associated with nephrolithiasis and therefore the Renal Stone waiver guide should be consulted in relevant patients. If renal function is affected or hypertension develops, as can happen particularly with PCKD, those waiver guides should also be consulted.

AIMWTS search in May 2019 for the prior 5 years revealed a total of 46 cases submitted with a diagnosis of medullary sponge kidney, horseshoe kidney, polycystic kidney, atrophic or congenitally missing kidney, congenital obstruction of ureteropelvic junction, renal ptosis, ectopic kidney, and other miscellaneous congenital kidney or ureteral obstructions. There were 4 FC I/IA cases, 22 FC II cases, 17 FC III cases, 2 ATC/GBC cases, and 1 MOD. There were 4 waivers for medullary sponge kidney (2 indefinite), 10 waivers for horseshoe kidney (4 indefinite), 15 cases with PCKD (2/15 disqualified), 10 waivers for agenesis or hypoplasia (2 indefinite), 6 waivers for congenital obstructions, and 1 case with ectopic kidney (1/1 disqualified). There were no waivers for nephroptosis. The one submitted case for ectopic kidney had prominent chronic kidney disease and another aeromedically-significant diagnosis resulting in disqualification. The other two disqualifications, both FC III, occurred in members with PCKD, hypertension, and other significant comorbidities. One was approved previously but had developed other pathology with significant aeromedical effects. Three FC II waivers were categorical, two for concurrent significant renal calculi and one for concurrent diabetes mellitus.

| ICD-9 codes fo | ICD-9 codes for Disease/Condition                            |  |  |
|----------------|--|--|--|
| 593.0          | Nephroptosis   |  |  |
| 753.0          | Absence of kidney  |  |  |
| 753.12/13      | Polycystic Kidney  |  |  |
| 753.17         | Medullary Sponge Kidney                                      |  |  |
| 753.19         | Other specified cystic kidney disease                        |  |  |
| 753.20         | Unspecified obstruction of renal pelvis and ureter           |  |  |
| 753.21         | Atrophic kidney  |  |  |
| 753.3          | Other specified anomalies (horseshoe kidney, ectopic kidney) |  |  |

| ICD-10 codes for Disease/Condition |  |
|------------------------------------|--|
| N28.83                             | Renal Agenesis, unilateral                           |
| Q60.0, Q60.2                       | Renal Agenesis, unilateral                           |
| Q61.2                              | Polycystic Kidney, adult type                        |
| Q61.5                              | Medullary Sponge Kidney                              |
| Q61.8                              | Other cystic kidney diseases                         |
| Q61.9                              | Cystic kidney disease, unspecified                   |
| Q62.39                             | Other obstructive defects of renal pelvis and ureter |
| Q60.3, Q60.5                       | Renal hypoplasia, unspecified                        |
| Q63.1                              | Lobulated, fused, and horseshoe kidney               |
| Q63.2                              | Ectopic kidney                                       |

# **IV. Suggested Readings**

- 1. Reynard J, Biers S, and Brewster S. Miscellaneous urological disease of the kidney. In *Oxford Handbook of Urology*. 3<sup>rd</sup> ed., Oxford University Press; 2013.
- 2. Simms RJ. Autosomal dominant polycystic kidney disease. BMJ, 2016; 352(8044): 243-47.
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### WAIVER GUIDE

*Updated: Dec 2015* 

Supersedes Waiver Guide of Mar 2011

By: Dr Dan Van Syoc

Reviewed by: Lt Col Eddie Davenport, Chief ACS Cardiologist

### **CONDITION:**

**Coronary Artery CalciumTesting (Dec 2015)** 

### I. Waiver Consideration.

Any degree of coronary artery disease is disqualifying for all flying classes, to include ATC, GBO and SWA personnel. *CAC tests with a score of 10 or greater are considered abnormal and require waiver submission.* For the purpose of aeromedical disposition, scores of 0-9 are considered normal and therefore qualifying for all classes of flying duties. While a positive CAC test is a non-invasive assessment of the presence of CAD, we do not recommend local aeromedical cardiac catheterization for asymptomatic individuals. Aviators who received a CAC test as part of a local evaluation for <u>symptoms</u> suggestive of CAD should complete their evaluation as directed by the local cardiologist.

Table 1. Summary of CAC Test Scores and ACS Requirements

| CAC Score | Flying Class Waiver Potential Required ACS |                      | _  |
|-----------|--|----------------------|--|
|           |  |                      | Review and/or ACS                          |
|           |  | Waiver Authority     | Evaluation                                 |
| 0-9       | FC I/IA, II and III                        | No waiver necessary† | No   |
| 10-99     | FC I/IA                                    | No                   | No   |
|           |  | AETC                 |  |
|           | II, GBO, SWA and                           | Yes                  | Yes - evaluation                           |
|           | III  | MAJCOM               | initially and every 1-2 years thereafter*# |
| 100-399   | FC I/IA                                    | No                   | No   |
|           |  | AETC                 |  |
|           | II, GBO, SWA, and                          | Yes                  | Yes - evaluation                           |
|           | III+                                       | MAJCOM               | initially and                              |
|           |  |                      | annually*#                                 |
| 400+      | FC I/IA                                    | No                   | No   |
|           |  | AETC                 |  |
|           | II, GBO, SWA, and                          | Yes                  | Yes - evaluation                           |
|           | III+                                       | MAJCOM               | initially with                             |
|           |  |                      | mandatory cardiac                          |
|           |  |                      | catheterization; re-                       |
|           |  |                      | evaluation dictated as                     |
|           |  |                      | per results#                               |

<sup>†</sup> Reminder: All cardiology tests (e.g., Holter, CAC testing, echocardiogram, ECG, treadmill, cardiac catheterization) on FC I/IA, FC II and GBO personnel must be sent to the ECG library. Call the ACS for the correct mailing address for the ECG Library.

AIMWTS search in Dec 2015 revealed nine cases with a code indicating that coronary artery calcium testing led to a diagnosis. Breakdown revealed 1 FC IA cases, 7 FC II cases (3 disqualified) and one FC III case. One of the three disqualified cases was due to TIAs and the other two were for multiple medical issues. It is estimated that there are many more cases in which coronary artery calcium testing was accomplished, but it was not captured in the diagnosis section of AIMWTS.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>\*</sup> Need for cardiac catheterization will be based on CADE (coronary artery disease equation) score at the ACS evaluation.

<sup>#</sup> If cardiac catheterization accomplished then follow Coronary Artery Disease waiver guide.

<sup>+</sup> Waiver for untrained FC II and III unlikely.

The aeromedical summary for <u>initial waiver</u> should contain the following information:

- A. Complete history and physical examination to include detailed description of any symptoms, exercise history, and CAD risk factors (positive and negative). <u>Also include</u> the reason the CAC test was obtained.
- B. Report of the CAC score. (Notes 1 and 2)
- C. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. echocardiography, treadmill, nuclear stress imaging). (Notes 1 and 2)
- D. Additional local cardiac testing is not routinely required but may be requested in individual cases.

The aeromedical summary for <u>waiver renewal</u> for abnormal coronary artery calcium should include the following:

- A. History brief summary of previous CT results and findings at ACS. Address interim cardiac symptoms (including negatives), exercise/activity level, and coronary artery risk factors and any medications.
- B. Local follow-up cardiac testing is not routinely required prior to ACS re-evaluation. If requested for individual cases, it will have been specified in the report of the previous ACS evaluation.
- C. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. Holter, treadmill, stress echocardiogram). (Notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840

2510 Fifth Street

WPAFB, OH 45433-7913

For expediting the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

### III. Overview.

Coronary artery calcium (CAC) testing has recently emerged as a powerful non-invasive assessment of the future risk of coronary heart disease and related events. Some recent studies have indicated that it is a great tool to predict coronary stenosis of greater than 50 percent. The test is commonly misused and results misinterpreted, however, leading to confusion in the clinical and aeromedical arenas.

The pathophysiology of coronary artery calcium is deceptively simple. When cholesterol deposits in the arterial wall, the typical physiological response is an outward thickening of the wall such that the cross-sectional area of the lumen is preserved (positive remodeling).<sup>3</sup> Some of these arterial atheromas undergo a process of calcification. These calcium deposits, if significant enough, can be seen with x-ray-based imaging such as routine chest x-rays, fluoroscopy, and computed tomography (CT scans). In the absence of arterial plaque, however, there is no opportunity for calcification in the arterial wall.

<u>Thus, the presence of any amount of coronary artery calcium confirms the presence of atherosclerotic coronary heart disease.</u> As such, CAC-testing is simply a non-invasive assessment of the presence of coronary heart disease. It is important to note that while the presence of CAC confirms the diagnosis of coronary heart disease, the converse is not true: it is possible to have coronary atheromas that have not calcified and thus are not detected by this type of testing.

CT-based tests for CAC have emerged as a powerful predictor of future coronary heart events.<sup>5</sup> Although there are many different CT-based types of CAC tests (electron beam CT [EBCT], multi-slice CT [MSCT], multi-detector CT [MDCT], multi-row CT [MRCT]), all produce a unit-less number which correlates to the amount of coronary artery calcium detected. Scoring of the amount of coronary calcium detected has been standardized and is highly reproducible amongst the different CT types and in serial studies. Thus, the higher the number, the greater the amount of calcification detected, and the greater the overall burden of coronary disease.<sup>6</sup> The reported CAC score is a total CAC burden, the sum of the scores of all individual calcium deposits. Recent data has emerged illustrating that even minor amounts of detectable coronary artery calcium result in significant coronary event rates, while more substantial CAC results in higher event rates.<sup>7,8</sup> This predictive value of CAC testing is particularly useful for younger, asymptomatic populations with low to moderate Framingham risk profiles.<sup>5</sup> In particular. recent studies have noted that in a healthy cohort of roughly 2,000 active-duty army personnel, the presence of any amount of detectable coronary artery calcium increased coronary heart events by nearly 12-fold. All the events in this cohort occurred in personnel between ages 40 and 50 years old with a Framingham risk score less than 10%, and with CAC scores as low as 10. Of interest, the appears to be no correlation between coronary calcium and the physiologic or anatomic significance of a stenosis.<sup>9</sup> Note that because this is a direct anatomic assessment, the typical false-positive and false-negative concerns associated with traditional cardiac testing do not apply. Rather, CT-based CAC testing is best viewed as a direct radiologic assessment of abnormal structures. The most recent American College of Cardiology and American Heart Association assessment of cardiovascular risk states that the CAC score is strong predictor of actual coronary artery disease.10

The Aeromedical Consultation Service (ACS) has been using the assessment of coronary artery calcium in its non-invasive assessment of aviators since 1982 (cardiac fluoroscopy). In-house data derived from a cohort of almost 1500 aviators with complete invasive and non-invasive assessments revealed that the presence of coronary artery calcium was the test most predictive of future cardiac events. Thus, current aeromedical policy ties the decision of whether to proceed to cardiac catheterization heavily to the presence of detectable CAC. The published data of comparable clinical cohorts with CT-based CAC testing reveal event rates of roughly 1% per year for individuals with a CAC score of 10 to 99, 2% per year for scores of 100-399, and above 3% per year when the CAC score is 400 or greater. These event rates mirror the event rates in the ACS database for aviators with angiographically proven minimal coronary artery disease (CAD), moderate CAD, and severe CAD, respectively.

#### IV. Aeromedical Concerns.

Because CAC testing is an anatomic assessment of the presence of CAD, and because the event rates for individuals with abnormal CAC tests mirror those of aviators with angiographically proven CAD, the aeromedical concerns surrounding abnormal CAC tests are the same as those for individuals with angiographically proven asymptomatic CAD. The major aeromedical concerns are myocardial ischemia presenting as sudden cardiac death, acute myocardial infarction, stable or unstable angina, or ischemic dysrhythmias, any of which could cause sudden incapacitation or significantly impair flying performance or mission completion. Additional concerns surround the need for invasive cardiac procedures and revascularization, frequent contact with cardiac specialists, and comprehensive medication regimens. At present, there is no reliable method of detecting asymptomatic progression of CAD short of frequent noninvasive monitoring, combined with periodic invasive testing.

| ICD9 code for coronary artery calcium testing |   |
|---|---|
| V81.2   | Special screening for other and unspecified cardiovascular conditions |

| ICD10 code for coronary artery calcium testing |  |
|--|--|
| Z13.6  | Encounter for screening for cardiovascular disorders |

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### **WAIVER GUIDE**

Updated: Dec 2015

Supersedes Waiver Guide of Mar 2012

By: Lt Col Hui Ling Li (RAM 16) and Dr Dan Van Syoc

Reviewed by: Lt Col Eddie Davenport, Chief ACS Cardiologist

### **CONDITION:**

**Coronary Artery Disease (Dec 2015)** 

### I. Waiver considerations.

Coronary Artery Disease (CAD) is disqualifying for all classes of flying duties to include GBO, ATC, and SWA personnel. CAD is disqualifying for retention if associated with myocardial infarction, major rhythm disturbances, congestive heart failure, angina, silent ischemia or for maintenance on any medication for prevention of angina, CHF or rhythm disturbance. Waiver is not recommended for FC I/IA or for unrestricted FC II/III duties. Severity of disease is defined below and categorized as Luminal irregularities only (LI), Mild or minimal (MinCAD), Moderate (MODCAD) or Severe (SCAD). Depending on the severity and extent of disease, waiver may be considered for categorical FC II/III duties (restricted to low performance aircraft defined as <2.5 sustained +Gz). Waiver may be considered for Initial FC II for Flight Surgeons, but will be similarly restricted. The only exception is that luminal irregularities (LI) only may be considered for unrestricted FC II/III duties. Additionally, modifiable risk factors must be acceptable, including but not limited to no use of tobacco products, no diabetes, controlled hypertension (per ACC/AHA guidelines), acceptable lipid profile (treated or untreated per ACC/AHA guidelines), and compliance with medications. These risk factors **must** be acceptable to both gain and maintain the waiver. Degree of coronary

Table 1: Summary of CAD Categories and ACS Requirements

| CAD Category             | Flying Class Waiver Required ACS |           |                          |
|--------------------------|----------------------------------|-----------|--------------------------|
| Classification           | • 0                              | Potential | Review and/or ACS        |
|                          |                                  |           | Evaluation               |
|                          |                                  | Waiver    |                          |
|                          |                                  | Authority |                          |
| Luminal irregularities   | FC II/III                        | Yes       | ACS evaluation           |
| (LI) only (no graded     | ATC/GBO/SWA                      | MAJCOM    | initially and four years |
| % stenoses) \$*          |                                  |           | later, then every two    |
|                          |                                  |           | years**                  |
| MinCAD\$#                | FC IIA rated aviators            | Yes       | ACS evaluation           |
| Aggregate <50%           |                                  | AFMRA     | initially and annually   |
| No left main disease     |                                  |           |                          |
|                          | GBO                              | Yes       | ACS evaluation           |
|                          | ATC                              | MAJCOM    | initially and            |
|                          | SWA                              |           | annually**               |
|                          | Restricted FC III                |           |                          |
| ModCAD\$+@               | FC IIC pilots                    | Yes       | ACS evaluation           |
| Aggregate $\geq$ 50% and | FC IIA navigators & flight       | AFMRA     | initially and annually   |
| <120%, and/or any        | surgeons                         |           |                          |
| gradable left main       | Restricted FC III                |           |                          |
| disease                  |                                  |           |                          |
|                          | GBO/ATC                          | Yes       | ACS evaluation           |
|                          | SWA                              | MAJCOM    | initially and annually   |
| SCAD\$∫                  | All Flying Classes               | No        | N/A                      |
| Aggregate $\geq$ 120% or |                                  | AFMRA     |                          |
| max lesion >70% or       |                                  |           |                          |
| left main ≥50%           |                                  |           |                          |
| Any CAD                  | FC I and FC IA                   | No        | N/A                      |
|                          | Initial FC II/III, SWA,          | AETC      |                          |
|                          | ATC, and GBO                     |           |                          |

<sup>\*</sup> Luminal irregularity only is eligible for unrestricted FC II/III waiver.

Individuals with a waiver for LI only will be reevaluated at the ACS four years after diagnosis, then every two years thereafter. Individuals with a waiver for MinCAD and ModCAD will be reevaluated at the ACS annually. Successful modification of cardiac risk factors must be demonstrated for LI only, MinCAD and ModCAD. Additional criteria for waiver of LI only and MinCAD include, but may not be limited to: no history

<sup>\*\*</sup> ACS annual evaluation not required for LI or MinCAD for ATC/GBO/SWA personnel unless requested by waiver authority.

<sup>#</sup> MinCAD is eligible for FC IIA waiver.

<sup>+</sup> ModCAD is eligible for FC IIC waiver for pilots, limited to low performance aircraft with another qualified pilot. For navigators and flight surgeons, waiver is FC IIA.

<sup>@</sup> MinCAD and ModCAD are eligible for restricted FC III waiver, limited to low performance aircraft.  $\int$  SCAD (aggregate  $\geq$ 120%) is disqualifying without waiver recommended. SCAD with a maximum lesion  $\geq$ 70% (SCAD>70) and CAD with a left main coronary lesion  $\geq$ 50% are also disqualifying without waiver recommended.

<sup>\$</sup> No indefinite waivers

suggestive of ischemic symptoms, no prior cardiac events (e.g. unstable angina, myocardial infarction) and normal left ventricular function. Repeat coronary angiography will not be required for LI only or for MinCAD in the absence of any suggestion of CAD progression or symptoms suggestive of ischemia. Additional criteria for waiver of ModCAD include, but may not be limited to: only one lesion of 50-70% stenosis, normal nuclear stress imaging study in the distribution of the 50-70% lesion, no history suggestive of ischemic symptoms, no prior cardiac events (e.g. unstable angina, myocardial infarction) and normal left ventricular function. Follow-up coronary angiography will be performed for ModCAD every five years routinely, or sooner depending on degree of risk factor improvement, complexity of disease, or for symptoms suggestive of ischemia or deterioration in noninvasive testing.

AIMWTS review in Dec 2015 revealed a total of 246 cases with known coronary artery disease. This total includes those with MI and revascularization as well. Breakdown of cases was as follows: 160 FC II cases (56 disqualifications), 75 FC III cases (29 disqualifications), 6 ATC/GBC cases (2 disqualifications), and 5 MOD cases (2 disqualifications). Of the total of 89 disqualified cases, the vast majority were disqualified primarily for cardiac disease.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> for coronary artery disease should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, blood pressure, medications, and activity level.
- B. Cardiology consult.
- C. Electrocardiogram (ECG).
- D. Report and CD copy of coronary angiography to the ACS. (Notes 1 and 2)
- E. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- F. Results of MEB or worldwide duty evaluation (for ARC members), if required (e.g. on medications or MI, etc.).

The AMS for waiver <u>renewal</u> should contain the following information:

- A. Complete history and physical exam to include description of any symptoms, medications, and activity level.
- B. Electrocardiogram (ECG).
- C. Additional local cardiac testing is not routinely required for re-evaluation cases followed at the ACS but may be requested in individual cases. If so, the previous ACS evaluation/review will specify details regarding any requested local testing.

D. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

This waiver guide addresses only <u>asymptomatic</u> coronary artery disease that has <u>not</u> been treated by revascularization (e.g. stent, bypass surgery). Refer to the Coronary Artery Revascularization waiver guide for revascularization cases.

Coronary artery disease (CAD) is the result of coronary artery plaque development, reducing oxygen supply to the myocardium.<sup>1</sup> It is the leading cause of death and premature, permanent disability of American males and females.<sup>2,3</sup> It accounts for approximately 16% of all deaths each year.<sup>4</sup> In spite of tremendous progress regarding CAD therapy, about 50% of initial and recurrent acute events continue to be fatal. Risk factors included older age, male sex, hypertension, hyperlipidemia, diabetes, obesity, smoking, and sedentary lifestyle.<sup>5,6</sup> Initial symptoms may include incapacitating angina, dyspnea, arrhythmia with altered consciousness or sudden death. Heat stress, hypoxia, high +Gz maneuvers and other features of the unique military cockpit/aircraft environment may provoke ischemia in individuals with pre-existing coronary artery lesions. CAD is the leading cause of disqualification for aviators.<sup>7</sup>

Coronary angiography is the golden standard for determining the presence and extend of CAD.<sup>6</sup> Clinically, significant CAD is defined as one or more lesions with  $\geq$ 50% stenosis (diameter reduction) by coronary angiography.<sup>7</sup> In the clinical literature, such disease is nearly always symptomatic, since it would rarely be identified otherwise. When treated medically, patients with this degree of disease are reported to show >5% per year annual cardiac event rates in favorable prognostic subgroups. Although the term significant coronary artery disease (SCAD) has historically also been applied to aviators discovered to have a maximal stenosis  $\geq$ 50%, event rates encountered in the clinical population may not accurately predict prognosis in the younger and relatively healthier aviator population with *asymptomatic* CAD.

To evaluate the actual risk associated with asymptomatic CAD, the Aeromedical Consultation Service (ACS) analyzed initial and long-term follow-up data from approximately 1,500 asymptomatic military aviators with coronary angiography. For

aviators with SCAD as defined above, average annual cardiac event rates exceeded 2.5% per year at 2, 5 and 10 years of follow-up. To further stratify risk, the SCAD group was divided into two subsets of SCAD severity, SCAD50-70 (worst lesion 50-70%) and SCAD>70 (worst lesion >70%). Detailed examination of the SCAD50-70 subset revealed that extent of disease (aggregate of lesions) at the time of index coronary angiography could further be stratified into a low-risk versus high-risk subjects. This new stratification used an aggregate of lesions defined as the arithmetic sum of all graded lesions, e.g. 60% lesion + 20% lesion + 30% lesion = aggregate of 110%. Aggregate <120% identified a lower-risk SCAD50-70 subgroup with an average annual event rate <1% per year at ten years of follow-up. Subsequent analysis of the group with minimal coronary disease (MCAD, defined at that time as maximal stenosis <50%) also showed that aggregate was significantly predictive of events albeit low.

Because aggregate successfully stratified cardiac risk, all groups with any CAD (combined SCAD and MCAD) with a maximal lesion  $\leq$ 70%, was submitted to a similar analysis. In this combined group, aggregate was highly predictive of event-free survival (p<0.00004). Specifically, aviators with an aggregate <50% showed an average annual event rate of 0.6% per year, while those with an aggregate  $\geq$ 50% but <120% had an average annual event rate of 1.1% per year. (Although a rate of 1.1% slightly exceeds the 1%/year threshold, the data reviewed predated the routine use of lipid-lowering therapy for secondary prevention, which would be expected to reduce events by an additional 30-40%).

By way of comparison, clinical literature reports annual cardiac event rates of about 0.5% per year in general population studies of apparently healthy asymptomatic males aged 35-54 years. Similarly, follow-up studies of male subjects with normal coronary angiography, who in most cases presented with a chest pain syndrome, report annual cardiac event rates of 0.2-0.7% per year. Annual cardiac event rates in apparently healthy USAF aviators have been reported by the ACS as  $\leq$ 0.15% per year for males aged 35-54 years although more recent data approaches the expected 0.5% per year rate.

From this database analysis, the current aeromedical classification of asymptomatic CAD is based on aggregate, with minimal CAD (MinCAD) defined as an aggregate <50%, and moderate CAD (ModCAD) defined as an aggregate  $\ge50\%$  but <120%. Significant CAD is now defined as an aggregate  $\ge120\%$ . A demonstrated maximum lesion >70% is also considered SCAD.

Graded lesions in the left main coronary artery are treated more cautiously due to the unfavorable prognosis associated with left main disease. Left main coronary artery lesions <50% stenosis are defined as ModCAD, assuming that other criteria for that classification are met. Left main lesions  $\ge 50\%$  stenosis are considered SCAD.

An additional category of CAD was more recently identified from the ACS database – luminal irregularities (LI) only. LI only describes coronary angiography with irregular arterial edges due to atherosclerotic plaque but less than gradable 10-20% stenosis (diameter reduction). LI only represents a subset of CAD with event rates higher than

those with truly normal coronary angiography (smooth arterial edges). A review of the ACS database showed that aviators with LI only on coronary angiography had no events in the first five years after diagnosis. However, between 5 and 10 years follow-up, cardiac event rates were 0.54% per year compared to 0.1% per year for those with truly normal coronary angiography. This represents a risk similar to MinCAD in the first five years of follow-up.

### IV. Aeromedical Concerns.

The aeromedical concern is myocardial ischemia presenting as sudden cardiac death, acute myocardial infarction, stable or unstable angina or ischemic dysrhythmias, any of which could cause sudden incapacitation or significantly impair flying performance. At present, there is no reliable method of detecting asymptomatic progression of CAD short of frequent noninvasive monitoring, combined with periodic invasive testing.<sup>8</sup>

Because cardiac catheterization of asymptomatic aviators with abnormal noninvasive testing is only recommended if the risk of CAD exceeds a predetermined threshold, local catheterization of asymptomatic aircrew for aeromedical indications alone is strongly discouraged. Where catheterization is indicated for <u>clinical</u> reasons, then of course the aviator should be managed as any other clinical patient would be.

| ICD 9 Codes for Coronary Artery Disease |   |  |
|---|---|--|
| 414                                     | Other forms of chronic ischemic heart disease   |  |
| 414.0                                   | Coronary atherosclerosis                        |  |
| 414.8                                   | Other specified forms of chronic ischemic heart |  |
|   | disease   |  |
| 414.9                                   | Chronic ischemic heart disease, unspecified     |  |

| ICD 10 Codes for Coronary Artery Disease |  |  |
|--|--|--|
| I25.89                                   | Other forms of chronic ischemic heart disease    |  |
| I25.10S                                  | Atherosclerotic heart disease of native coronary |  |
|  | artery without angina pectoris                   |  |
| I25.9                                    | Chronic ischemic heart disease, unspecified      |  |

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### **WAIVER GUIDE**

Updated Jun 2016

Supersedes Waiver Guide of Aug 2012

By: Lt Col (Dr.) Paul De Florio, Lt Col (Dr.) Eddie Davenport (ACS Chief Cardiologist) and Dr. Dan Van Syoc

### **CONDITION:**

**Coronary Artery Revascularization (Jun 2016)** 

### I. Waiver Considerations.

Coronary artery disease and coronary artery revascularization are disqualifying for all classes of flying duty and retention. The events triggering revascularization are critical, as there is greatly increased morbidity and mortality in the setting of MI. If there is evidence of myocardial infarction (ECG changes, or cardiac enzymes elevation) then they must meet criteria for the myocardial infarction waiver policy. In general, revascularization should not be done for asymptomatic coronary artery disease. ACS review and evaluation is required for waiver consideration. Waiver restricted to low performance aircraft may be considered for all flying classes. Coronary artery revascularization is also disqualifying for ATC/GBO/SWA duty as well as for retention purposes, and MEB and waiver is required before return to duty.

Waiver for pilots, limited to FC IIC (low performance aircraft with another qualified pilot) was approved by the Aerospace Medicine Corporate Board in 2008. Criteria for waiver consideration for all aviators include (must meet all of the below):

- A. Normal left ventricular wall motion and systolic function,
- B. Complete revascularization; all lesions with  $\geq 50\%$  stenosis successfully treated,
- C. The sum of all remaining stenosis should be less than 120%,
- D. No reversible ischemia on noninvasive testing (off cardioactive medicines),
- E. For PCI, no restenosis over 50%,
- F. Successful risk factor modification,
- G. A minimum DNIF observation period of six months post procedure.

ACS evaluation for initial waiver consideration will include complete noninvasive testing and follow-up coronary angiography. If waiver is recommended and granted, waiver will be valid for one year with annual ACS re-evaluation required for waiver renewal consideration. In addition, routine serial coronary angiography *is required at five year intervals*. Follow-up coronary angiography may be recommended sooner if indicated by symptoms, noninvasive test results, or failure to control risk factors.

**Table 1: Coronary Artery Revascularization and Waiver Potential** 

| Flying Class         | Waiver Potential | ver Potential ACS  |  |
|----------------------|------------------|--------------------|--|
|                      | Waiver Authority | Review/Evaluation  |  |
| I/IA                 | Not Waiverable   | NA                 |  |
| II (unrestricted)    | Not Waiverable   | NA                 |  |
| IIA (flight surgeon) | Yes*             | Yes, Annual        |  |
| IIC (pilot)          | AFMRA            |                    |  |
|                      |                  |                    |  |
| III                  | Yes*             | Yes, Annual        |  |
|                      | MAJCOM**         |                    |  |
| ATC/GBO/SWA          | Yes*             | Review possible*** |  |
|                      | MAJCOM**         |                    |  |

<sup>\*</sup> Must meet following criteria for consideration: 100% revascularization, <50% single lesion, <120% aggregate, normal LVEF, no wall motion abnormality. Adequate medical management may include statin, aspirin, nitroglycerin, and/or ACE inhibitor, as clinically appropriate. Additionally, patient must have controlled hypertension, no diabetes, no other significant co-morbidities, and controlled risk factors. Low performance aircraft defined as <2.5 sustained G, with another qualified pilot. No altitude restriction in low performance aircraft.

AIMWTS review through Jun 2016 revealed 143 submitted cases with a history of revascularization. There were 0 FC I/IA cases; 89 FC II cases (39 disqualified), 48 FC III cases (18 disqualified); 4 ATC/GBC cases (disqualified); and two MOD cases (one disqualified).

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for coronary artery revascularization should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of CAD and procedures.
- C. Consultation notes from a cardiologist.
- D. Imaging: Copy of the cardiac catheterization report and copy of the images (CD, cineangiogram or videotape); copy of the revascularization procedure report (CABG or PCI) and for PCI copy of the images (CD, cineangiogram or videotape); copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. electrocardiogram, treadmill, nuclear myocardial stress perfusion imaging).
- E. Additional local cardiac testing is not routinely required, but may be requested in individual cases. Copies of reports of any such testing will be required.
- F. Results of MEB returning member to worldwide duty.

<sup>\*\*</sup> AFMRA is the waiver authority for all initial waivers.

<sup>\*\*\*</sup> Annual testing may be done locally and sent to ACS for review at the request of the MAJCOM, alternatively all testing and follow-up can be done during annual ACS evaluations.

The AMS for <u>waiver renewal</u> for coronary artery revascularization should include the following:

A. Interval history since last waiver.

B. All applicable and imaging tests and reports that have been completed since last waiver/renewal. If annual ACS evaluation is required, no local testing is required unless clinically indicated as follow-up testing will be done at annual ACS evaluation.

C. Consultation (any follow-up exams) from local cardiologist.

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB. OH 45433-7913

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

### III. Overview.

Coronary artery revascularization addresses occlusive coronary artery disease (CAD) via either coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI), which most commonly includes the catheter-based techniques of angioplasty and stent placement. Because these techniques are palliative, not curative, any new cardiac events 6-12 months after successful revascularization are primarily caused by progression of disease.<sup>1</sup>

Two large trials with long term follow up were designed to compare outcomes of PCI versus CABG.<sup>2-3</sup> With a median follow up of 4.6 years, the BEST trial measured a primary end point of death, myocardial infarction (MI), and target-vessel revascularization. The PCI group rate was 15.3%, and the CABG rate was 10.6% at 4.6 years.<sup>3</sup> The SYNTAX trial reported five year event data, with a composite end point of death, MI, stroke, and repeat revascularization. Their PCI group suffered events at a rate of 37.3%, with the CABG group reported as 26.9%.<sup>2</sup> For both trials revascularization drove the primary endpoint and neither death nor MI were independently significantly different with MI and mortality rates of approximately less than 2% per year. Kaplan-Meier curves in both trials also showed an early spike in complication rates, with a more linear curve after 6-12 months, which reinforces historical waiver guide recommendations that patients only be assessed after a minimum of six months post-procedure. Although both trials favor CABG over PCI, it is important to note this was driven by target vessel revascularization and reinforces policy that either CABG or PCI can be done in aviators. Data with newer-generation drug-eluting stents is ongoing.

The applicability of these and similar trials to the military aviator is very limited, as they universally study older patients with high rates of comorbidities. In addition, they also

record post-intervention complications that fall within the first 6-12 months, which would not be applicable to military aviators. In an attempt to address these shortcomings, one older study re-examined the large post-CABG database and extracted a "simulated aviator population" of males under 60 with no history of cardiovascular comorbidities and no major complications within 12 months. Of these, the two youngest cohorts (ages 20-39 and 40-49) best resemble the military aviator population. Their five year cardiac event-free rate was found to be 94 +/-3% and 91 +/-2% respectively.<sup>4</sup>

A retrospective review of ACS data studied 122 former military aviators with no prior cardiac events who underwent coronary artery revascularization.<sup>5</sup> About half the group had CABG and the other half had PCI, primarily angioplasty. There were no cardiac deaths within five years and only two myocardial infarctions, both beyond two years follow-up. After excluding repeat revascularization within six months of the index revascularization, cardiac event rates at one, two, and five years were 1.0%, 2.7% and 3.6% per year respectively. Individuals meeting the below waiver criteria have estimated cardiac event rates of 2-3% per year for up to five years after revascularization.

Recently a selected group of 30 aviators that presented to ACS (2000-2008) while on active duty, after having had coronary revascularization, were chosen for a retrospective study to determine the time to event and resulting annual event rate. Out of these, only two progressed requiring revascularization. There were no deaths and no MIs. The annual event rate was 2.1% (CI 1.2% - 3.0%). The event free survival was 97% at two years and 88% at 5 years. Both of these patients needing repeat intervention would likely have been identified during the annual ACS reevaluation as required by policy. Neither would have manifested as an incapacitating event.

### IV. Aeromedical Concerns.

The aeromedical concern is myocardial ischemia presenting as sudden cardiac death, myocardial infarction, angina or ventricular dysrhythmias, all of which may cause sudden incapacitation or seriously impact performance of flight duties. Detecting the asymptomatic progression of CAD reliably without frequent invasive testing or noninvasive monitoring is the aeromedical challenge.

| ICD-9 Codes for coronary artery disease |                                     |
|---|-------------------------------------|
| 414.00                                  | Coronary artery disease             |
| 36.10                                   | Coronary artery bypass graft (CABG) |
| 36.06                                   | Coronary artery stent placement     |
| 36.09                                   | Coronary artery angioplasty         |

| ICD-10 Codes for coronary artery disease |  |
|--|--|
| I25.10                                   | Coronary artery disease without angina |
| Z95.1                                    | Coronary artery bypass graft (CABG)    |
| Z98.61                                   | Coronary artery angioplasty with or    |
|  | without stent placement                |

### V. References.

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# Crohn's Disease (Apr 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

**Significant Changes**: Waiver guide updated to reflect national guidelines, waiver requirements updated, career field-specific approved medications clarified, and aeromedical concerns section expanded

### I. Waiver Consideration

Crohn's disease is disqualifying for all flying classes, ground-based operators, and other special duty operators as well as for retention. Aeromedical waiver is usually not recommended for untrained personnel. Factors considered when assessing suitability for aeromedical waiver include the severity of disease at diagnosis, evidence of clinical and endoscopic remission, whether treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the risk associated with specific medication(s), the individual service member's tolerance of the medication(s) and adherence to therapy, and the cumulative risk of all associated complications and/or extraintestinal manifestations. Individuals not on an appropriate treatment regimen will not be considered waiver-eligible. Waiver can be considered once an aviator is in disease remission on a stable, aeromedically-approved medication regimen, without adverse effects. Use of any medication not included on the career field approved medication list is independently disqualifying and will be considered on a case-by-case basis.

Individuals who demonstrate clinical but not endoscopic remission will not be considered waiver-eligible due to studies that show a higher risk for symptomatic recurrence when there is persistent disease on endoscopy. For aeromedical purposes, endoscopic remission is assessed either after completion of treatment or while on maintenance therapy and is defined as visual (i.e., esophagogastroduodenoscopic or colonoscopic) and histologic (i.e., tissue biopsy) demonstration of mucosal healing without evidence of active inflammation.

Crohn's disease with small bowel involvement, including disease of the ileocolon, is more likely to result in intestinal complications and is more difficult to treat than isolated Crohn's disease of the colon. Computed tomography enterography (CTE) or magnetic resonance enterography (MRE) are often used during the initial evaluation to assess for the presence of small bowel disease. Prior to consideration for an aeromedical waiver, individuals with a history of small bowel involvement must demonstrate at least six months of asymptomatic stability and be without active intestinal complications (i.e., strictures, abscesses, or fistulas). Individuals with more than two prior surgeries for Crohn's disease will not be considered for waiver due to the high risk for future complications. Initial waivers for trained pilots with small bowel involvement and less than 12 months of demonstrated asymptomatic stability will be restricted to multiplace aircraft with another qualified pilot. In pilots granted an initial restricted waiver, reconsideration for an unrestricted aeromedical waiver can be entertained after 12 months of asymptomatic stability.

Table 1: Waiver potential for Crohn's disease

| Flying Class (FC)         | Condition   | Waiver Potential <sup>1</sup> Waiver Authority | ACS Review or Evaluation |
|---------------------------|---|--|--------------------------|
| I/IA                      | Crohn's disease of any degree   | No<br>AETC                                     | N/A                      |
| II//III<br>GBO/ATC<br>SWA | Crohn's disease isolated to colon <sup>2,3,4</sup>  | Yes<br>MAJCOM                                  | Yes                      |
|                           | Crohn's disease with small bowel involvement (i.e., proximal GI, terminal ileum, or ileocolonic) <sup>2,3,4,5</sup> | Yes<br>MAJCOM                                  | Yes                      |

- 1 Untrained personnel of any class are unlikely to receive aeromedical waiver, and ACS review/evaluation is not necessary.
- Waiver consideration is based on clinical remission, endoscopic remission, appropriateness of treatment, and whether disease remission can be maintained with career field-specific approved medications. Use of any medication not included on the career field-specific approved medication list is independently disqualifying and will be considered on a case-by-case basis (see section III. Aeromedical Concerns).
- 3 Clinical and endoscopic remission is required prior to waiver consideration. For aeromedical purposes, endoscopic remission is assessed either after completion of treatment or while on maintenance therapy and is defined as visual (i.e., colonoscopic) and histologic (i.e., tissue biopsy) demonstration of mucosal healing without any evidence of active inflammation.
- 4 Individuals treated with TNF-alpha inhibitors will be considered for a restricted waiver (not worldwide qualified, TDY requires access to transport, and refrigeration of medication) if found fit for military retention, and waiver authority is AFMRA.
- Individuals with small bowel involvement must be asymptomatic for six months, have no active intestinal complications (i.e., stricture, abscess, fistulas), or more than two prior surgeries. Pilots with small bowel involvement will initially be considered for a restricted waiver to multiplace aircraft with another qualified pilot. An unrestricted waiver for pilots with small bowel involvement can be considered after 12 months of asymptomatic stability.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- 2. Consultation reports from all treating providers or specialists, which should include:
  - a. Subjective symptoms and objective physical exam findings.
  - b. Current treatment plan, to include tolerance and current doses of maintenance medications and all appropriate monitoring labs for those

- medications, as applicable (e.g., biologic agents require CBC/CMP every 3-6 months and annual TB testing).
- c. Documentation excluding/including extra-intestinal manifestations (e.g., ankylosing spondylitis, anterior uveitis, primary sclerosing cholangitis, etc.).
- d. Documentation of any complications; i.e, fistula, abscess, stricture, and whether surgical intervention has ever been required.
- 3. Results of all pertinent laboratory studies, including diagnostic and follow-up results. Must include recent CBC, CMP, ESR, and CRP.
- 4. Radiology reports from all diagnostic or follow-up imaging studies (including CTE or MRE).
- 5. All endoscopy and biopsy reports, including results of repeat endoscopy while clinically stable demonstrating endoscopic remission.
- 6. Current physical examination findings.
- 7. FL4 with RTD and ALC status.
- 8. Any other pertinent information.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - Current symptoms and development of any disease flares, complications, or extra-intestinal manifestations.
  - b. Current medications, doses, and adverse effects.
  - c. Current physical examination findings.
- 2 Consultation reports from treating gastroenterologist or internist.
- 3 Any interval endoscopy reports with biopsy results.
- 4 Updated CBC, CMP, ESR, and CRP.
- 5 Any other pertinent information.
- If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

### III. Aeromedical Concerns

Crohn's disease is chronic, relapsing and remitting inflammatory disease potentially affecting any site of the gastrointestinal tract. The disease can be isolated to the small bowel (proximal gastrointestinal tract and/or terminal ileum), large bowel (colonic), or affect both the small and large bowel (ileocolonic). Disease severity is traditionally assessed using the Crohn's Disease Activity Index (CDAI), which utilizes subjective symptoms and objective data. For aeromedical purposes, CDAI is not routinely used; however, individuals seeking medical waiver should have no more than four bowel movements per day, no active intestinal complications, normal inflammatory markers, and no disease symptoms or side effects of treatment that would significantly impact aviation duties. Symptomatic and endoscopic remission is required prior to waiver submission, whether spontaneous or as a result of maintenance treatment with career field approved medications. Once clinical remission is achieved, endoscopic remission must be

confirmed prior to waiver consideration. Although repeat endoscopy to assess for mucosal healing is not always performed in clinical practice, the risk of disease flare or long-term complication is increased in individuals who do not achieve endoscopic remission, despite absence of symptoms. Given the unpredictability of Crohn's disease flares, individuals in remission who are not on maintenance therapy should be monitored for six months prior to waiver submission.

Uncontrolled or untreated Crohn's disease can result in distracting symptoms, such as diarrhea, abdominal pain, weight loss, and fatigue. Small bowel involvement increases risk of nutritional deficiencies such as iron deficiency and vitamin B12, which may contribute to the development of aeromedically significant anemia or peripheral neuropathy. Recurrent or persistent inflammation can lead to gastrointestinal complications such as strictures, abscesses, and fistulas. Intestinal complications, particularly stricture formation, increase the risk of small bowel obstruction, which may present acutely with sudden onset of severe and incapacitating symptoms. The aviation environment increases the risk of symptomatic small bowel obstruction due to gas expansion at altitude. For this reason, pilots with Crohn's disease flares involving the small bowel will require a restricted waiver. In those with small bowel involvement, the 10-year cumulative risk for requiring a major abdominal surgery is between 40 to 55%. However, newer data in the era of biologic therapy places this risk at closer to 30%. Recurrent abdominal surgeries increase the risk of small bowel obstruction. Thus, individuals with two or more surgeries involving the small bowel are unlikely to receive a waiver. Surgery is not considered curative. Provided that an individual is asymptomatic without surgical complication, ileostomy, or colostomy, an aeromedical waiver can be considered. Additionally, careful assessment for extra-intestinal manifestations of ulcerative colitis including anterior uveitis, primary sclerosing cholangitis, and arthritis should be performed.

Treatment for Crohn's disease is primarily directed toward the induction and maintenance of remission. Standard maintenance therapies for Crohn's disease include oral steroids (e.g., budesonide), 5-amiosalicylates (5-ASA), immunomodulators, or biologic agents. Currently, there are several 5-ASA preparations and two biologic agents (infliximab and adalimumab) that are approved for use in aviators, ground-based, or special duty operators. Oral steroids and immunomodulators such as azathioprine and 6mercaptopurine are not currently on any career-filed approved medication list due to the unacceptable adverse effect profile and/or need for frequent laboratory monitoring. However, azathioprine and 6-mercaptopurine are increasingly being used to induce and maintain remission in Crohn's disease. The most concerning aeromedical adverse effects of these medications are the development of myelosuppresion, pancreatitis, and/or hepatotoxicity. The highest risk of developing severe myelosuppression occurs within the first year of therapy. Testing for Thiopurine Methyltransferase (TPMT) genotype prior to initiating therapy is required to mitigate the risk of developing severe myelosuppression. In select unmanned aviation fields such as FCII-RPA or certain ground base operators who do not commonly deploy to an austere environment, azathioprine and 6mercatopurine could be considered for waiver on case-by-case basis.

Individuals who received treatment with exogenous steroids for greater than three weeks within the last year require aeromedical assessment of the hypothalamic-pituitary-adrenal axis prior to waiver consideration. Please refer to the Systemic Glucocorticoid (Steroid) Treatment waiver guide.

Review of AIMWTS data in Apr 2019 revealed a total of 25 waiver packages containing the diagnosis of Crohn's disease since Jan 2014. Of that total, 1 was FC I/IA (1 disqualified), 14 were FC II (1 disqualified), 6 were FC III (2 disqualified), 3 were ATC/GBC (1 disqualified), and 1 was MOD (0 disqualified). Disqualifications were due to either uncontrolled symptoms, use of unapproved career-field medications, or Crohn's disease related complications.

| ICD-9 codes for Crohn's Disease |  |
|---------------------------------|--|
| 555.0                           | Crohn's disease, small intestine         |
| 555.1                           | Crohn's disease, large intestine         |
| 555.9                           | Crohn's disease, not otherwise specified |

| ICD-10 codes for Crohn's Disease |   |  |
|----------------------------------|---|--|
| K50.0                            | Crohn's disease, small intestine                      |  |
| K50.1                            | Crohn's disease, large intestine                      |  |
| K50.8                            | K50.8 Crohn's disease, both small and large intestine |  |

## **IV. Suggested Readings**

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## **Decompression Sickness and Arterial Gas Embolism (Mar 2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Col Michael Richards (AF/SG Hyperbaric Medicine Consultant), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

**Updated Waiver Considerations and References** 

### I. Waiver Consideration

Decompression sickness (DCS) or air embolism (AGE) with neurologic involvement by history, physical examination or evidence of structural damage on imaging studies is disqualifying for FC I/IA, FC II, FC III and Operational Support Flying Duty. Current literature suggests it is rare for DCS symptoms to begin more than 36 hours following decompression exposure. However, DCS should still be considered in the differential diagnosis for individuals presenting with DCS symptoms beyond this period of time if there is history of a credible exposure to significant change in pressure (i.e. at or above 18,000 ft, scuba diving, or hyperbaric exposure). Hypobaric chamber-induced neurologic DCS/AGE with symptom resolution within 2 weeks does not require waiver. Any altitude-induced DCS/AGE episode that requires recompression therapy and symptoms are not resolved within two weeks requires a waiver. Current medical knowledge does not permit clear delineation of susceptibility to repeat DCS, nor does it allow precise definition of risk of sudden incapacitation or of neurocognitive impairment. As a consequence, the Aeromedical Standards Working Group (ASWG) recommended the following pending acquisition of data that will permit further refinement of risks: a minimum 72-hour DNIF period following clinical symptoms related to hypobaric chamber exposure, a minimum 2-week DNIF following an altitudinal exposure with complete resolution of symptoms within 2 weeks of exposure and with acceptable studies as listed below, and a minimum 6-month DNIF period following altitudinal exposure for symptoms persisting beyond 2 weeks or without acceptable studies as listed below. DCS is not disqualifying for ATC and GBO duties.

Table 1: Waiver potential for DCS and AGE

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------|------------------|--------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | Yes                      |
| FC II/III/OSD     | Yes <sup>1</sup> | MAJCOM/<br>AFMRA | Yes                      |

<sup>1.</sup> If symptoms completely resolve after more than 14 days, or any residual symptoms are not functionally-limiting, aeromedical waiver recommendation is likely.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable. Recompression by hyperbaric oxygen therapy is the definitive treatment for DCS and AGE.

Table 2 lists considerations for aeromedical waiver consideration after DCS or AGE.

Table 2: DCS/AGE return to flying status (RTFS) considerations

| 20010 20 2 0 0 7 1 | Tubic 20 D confided retain to my mg beatab (1111 b) complete actions |  |  |  |  |
|--------------------|--|--|--|--|--|
|                    | DCS/AGE with no CNS <sup>1</sup> or                                  | DCS/AGE categorized as severe, including     |  |  |  |
|                    | pulmonary involvement  | CNS <sup>1</sup> or pulmonary involvement    |  |  |  |
| Hypobaric          | No Waiver Required   | Waiver Required                              |  |  |  |
| chamber or         |  |  |  |  |  |
| altitude-          | May be RTFS by local flight  | Minimum 1-month DNIF following resolution    |  |  |  |
| induced            | surgeon after consultation with                                      | of all symptoms if all results below are     |  |  |  |
| DCS, with          | base SGP, USAFSAM Hyperbaric   | acceptable upon review by the ACS.           |  |  |  |
| all symptoms       | Medicine Branch and  | Minimum 6-month DNIF if all results below    |  |  |  |
| resolved           | MAJCOM/SGP. Requires a   | are not acceptable upon review by the ACS.   |  |  |  |
| within 2           | minimum 72-hour DNIF following                                       |  |  |  |  |
| weeks              | resolution of all symptoms.  |  |  |  |  |
| Altitude-          | Waiver Required  | Waiver Required                              |  |  |  |
| induced DCS        |  |  |  |  |  |
| with               | Symptom-focused evaluation by  | Requires a minimum 6-month DNIF with         |  |  |  |
| persistent         | appropriate specialty/specialties                                    | evaluation as listed below and review by the |  |  |  |
| symptoms           | and aeromedical disposition per                                      | ACS.   |  |  |  |
| beyond 2           | AFI  |  |  |  |  |
| weeks              |  |  |  |  |  |
|                    |  |  |  |  |  |

<sup>1.</sup> If peripheral neurological complaints are the sole presenting symptoms and if these symptoms completely resolve with recompression treatment, a full 2-week or 1-month DNIF is not warranted.

## A. Initial Waiver Request:

- 1. Complete history of event detailing risk factors, exposures, initial symptoms, treatment, any residual symptoms, signs and functional limitations.
- 2. Current physical, mental status and neurologic examinations performed by a Neurologist or Hyperbaric Medicine specialist.
- 3. Copies of relevant clinical notes (particularly consultation reports from Neurology, and Hyperbaric Medicine if obtained), and reports of diagnostic studies.
- 4. Neurocognitive testing at one month, to include the Multidimensional Aptitude Battery (MAB) and MicroCog tests, with results sent to ACS.
- 5. Noncontrast MRI studies (on minimum 1.5T MRI unit) within one month of episode, with report(s) and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 6. Documentation of any consultation with USAF Hyperbaric Medicine physician.
- 7. Chest x-ray (PA/lateral) to rule out lung parenchymal pathology in cases of pulmonary AGE.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

1 Interval history, including any residual symptoms, signs, and current functional status.

- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical, mental status and neurologic exam findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### III. Aeromedical Concerns

Aeromedical concerns include the effects of any residual neurologic or cognitive symptoms on operational safety and mission effectiveness, and future risk of recurrence. The pathophysiology of decompression illness is not entirely understood. The risk of recurrent injury or increased susceptibility to subsequent injury following an initial episode of DCS is unknown, as is the short and long-term risk of permanent neurocognitive impairment following repeated episodes of neurologic DCS. Permanent subcortical dementia following a single episode of neurologic DCS in an aviator has been documented in at least one ACS-assessed case. The risk of seizures from structural brain abnormalities following altitudinal DCS is unknown. An unexpectedly increased amount of subcortical white matter hyperintensities have been noted on brain MRI in some U-2 pilots and hypobaric chamber personnel, even in the absence of a history of neurologic DCS. The clinical significance, both immediate and long term, of these findings is currently unknown. A consensus statement from the 2010 DCS-AGE Workshop noted the risk of seizures is unknown, with currently no medical evidence indicating increased risk of seizure. Large-vessel occlusion from AGE in the aviation environment is rare. If it does occur, the pulmonary rupture that caused the AGE must completely heal before consideration of returning to flying duties. Furthermore, any pulmonary pathologic conditions that could predispose to recurrence should be excluded via radiographic studies.

Review of AIMWTS through Jan 2019 showed 48 cases of decompression sickness; seven received a disqualified disposition. Breakdown of the cases revealed: 2 FC I/IA cases (both disqualified), 27 FC II cases (1 disqualified), and 19 FC III cases (4 disqualified).

| ICD-9 codes for Decompression sickness |                 |  |
|--|-----------------|--|
| 993.3                                  | Caisson disease |  |
| 958.0                                  | Air embolism    |  |

| ICD-10 codes for Decompression sickness |                        |  |
|---|------------------------|--|
| T70.3 (generic)                         | Decompression Sickness |  |
| T70.3XXA (initial encounter)            | Aeroembolism           |  |
| T70.XXD (subsequent encounter)          |                        |  |
| T70.3XXS (sequelae)                     |                        |  |

## **IV. Suggested Readings**

- 1. Connolly DM, Lee VM, Hodkinson PD. White matter status of participants in altitude chamber research and training. Aerosp Med Hum Perform 2018; 89(9):777-786.
- 2. Cooper JS, Hanson KC. Aerospace, Decompression Illness. StatPearls, Mar 21, 2019. Link: https://www.ncbi.nlm.nih.gov/books/NBK537264/
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- 5. Hossack M, Sladky J, McGuire SA. A proposed mechanism of neuronal injury in pilots and aircrew personnel with hypobaric exposure. Neurology 2017; 88(16, Suppl):S53.005
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### **Diabetes Mellitus (Dec 2019)**

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**Significant Changes:** Updated to reflect most recent guidelines on the management of diabetes and co-morbid diseases, including the current *Standards of Medical Care in Diabetes* from the American Diabetes Association

### I. Waiver Consideration

Any type of diabetes mellitus is disqualifying for all flying duties, GBO duties, ATC duties and Special Warfare duties. It is also disqualifying for retention. Impaired fasting glucose, impaired glucose tolerance, or pre-diabetes mellitus are not considered disqualifying. However, treatment with metformin requires a waiver. Waiver requirements for diabetes mellitus or for the use of metformin generally follow the recommendations established in the most recent version of the "Standards of Medical Care in Diabetes," which is updated annually by the American Diabetes Association. Individuals who are not treated or monitored to recognized national or international standards of care will not be considered eligible for a waiver. Factors that are considered when assessing suitability for waiver include whether the treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the degree and stability of glucose control, the medication regimen and adherence to treatment, the cumulative risk of all comorbid conditions, and whether other metabolic or cardiovascular risk factors are present. These factors are also considered in determining whether a restricted or unrestricted waiver is appropriate.

The use of insulin to control blood glucose is considered incompatible with military aviation and enhanced operational duties due to the high incidence and frequency of serious hypoglycemic adverse effects. Therefore, a waiver will not be considered for service members who require insulin treatment. Thus, any person with type 1 diabetes mellitus and anyone with latent autoimmune diabetes in adults (LADA) or type 2 diabetes mellitus treated with insulin will not be considered waiver-eligible.

All waivers for LADA and diabetes mellitus type 2 are considered on a case-by-case basis. Due to the high risk for complications of aeromedical significance, FC I/IA waivers are unlikely to be granted for applicants with any history of diabetes mellitus. Waivers may be considered in low-risk individuals who are treated with other anti-hyperglycemic agents or for untrained FC II, FC III, GBO, ATC, and SWA candidates.

In addition to insulin, many of the medications used to treat diabetes mellitus convey side effects that are incompatible with aviation or enhanced operational duties. The only medications officially approved for use in USAF aviators, ground-based operators, or other special duty operators are metformin and sitagliptin. These medications were approved after careful reviews demonstrated that with appropriate restrictions, the risk of adverse effects of aeromedical consequence were acceptable, including the risk of both symptomatic and subclinical hypoglycemia. To appropriately mitigate risk, waivers for pilots treated with metformin and/or sitagliptin are typically restricted to FC IIC, dual-control aircraft with another qualified pilot.

A waiver request may be considered once a service member demonstrates at least 30 days of stability on an appropriate medication regimen without adverse effects. Blood glucose must be adequately controlled according to accepted national and international guidelines (generally, HbA1c less than 7%). Please refer to the complete list of requirements for waiver consideration in section II, "Information Required for Waiver Submittal."

**Table 1: Waiver potential for Diabetes Mellitus** 

| Flying Class (FC) | Condition   | Waiver Potential<br>Waiver Authority <sup>1</sup> | ACS Review or Evaluation |
|-------------------|---|---|--------------------------|
| I/IA              | Any history of diabetes mellitus<br>type 1 or type 2, regardless of<br>treatment (with the exception of<br>uncomplicated gestational<br>diabetes resolved after delivery) | No<br>AETC  | No                       |
| II/III            | Diabetes mellitus type 2 controlled through therapeutic lifestyle with/without approved medication (i.e., metformin and/or sitagliptin) <sup>2</sup>                      | Yes <sup>2</sup><br>MAJCOM                        | Yes                      |
|                   | Diabetes mellitus type 1 or 2, treated with insulin or any other non-approved antihyperglycemic agent <sup>3</sup>  | No <sup>3</sup><br>MAJCOM/AFMRA <sup>3</sup>      | No <sup>3</sup>          |
| GBO/ATC/SWA       | Diabetes mellitus type 2<br>controlled through therapeutic<br>lifestyle with/without approved<br>medication (i.e., metformin<br>and/or sitagliptin)                       | Yes<br>MAJCOM                                     | No                       |
|                   | Diabetes mellitus type 1 or 2,<br>treated with insulin or any other<br>non-approved anti-<br>hyperglycemic agent <sup>3</sup>   | No <sup>3</sup><br>MAJCOM/AFMRA <sup>3</sup>      | No <sup>3</sup>          |

AFMRA is the waiver authority for all initial waivers in untrained FC II, III, ATC, GBO, and SWA applicants.

Waivers for pilots treated with metformin and/or sitagliptin are typically restricted to FC IIC, dual-control aircraft with another qualified pilot.

Use of any medication that is not included on the approved medication list is disqualifying, and the MAJCOM may disqualify the service member without AFMRA or ACS review. Waiver may be considered following an ACS review on a case-by-case basis in certain low-risk individuals treated with alternative anti-hyperglycemic agents (e.g., GLP-1 receptor agonists, SGLT2 inhibitors). The waiver authority for all non-approved medications is AFMRA. Waiver will not be considered for insulin, and ACS review is not required.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

## A. <u>Initial Waiver Request:</u>

- 1. Summary of presentation, course, and treatment.
  - a. List all risk factors for metabolic syndrome and atherosclerotic cardiovascular disease (ASCVD)
    - i. Non-modifiable risk factors (age, gender, race/ethnicity, family history)
    - ii. Modifiable risk factors (tobacco use, current blood pressure, current lipid panel, personal history of treatment for hypertension or hyperlipidemia)
  - b. List all treatments trialed, their effectiveness, and any adverse effects
  - c. List current medications, doses, and adverse effects
    - i. At least 30-Days of medication regimen stability should be demonstrated
  - d. List all co-morbid conditions and describe degree of control
  - e. Document completion of a formal multi-disciplinary diabetes education program
- 2. Laboratory studies required:
  - a. Baseline blood glucose measurement and HbA1c level before starting treatment
  - b. Current fasting blood glucose measurement and HbA1c level
  - c. Baseline and current fasting comprehensive metabolic panel (CMP)
  - d. Current fasting lipid panel
  - e. Current quantitative spot urine albumin-to-creatinine measurement
  - f. If treatment includes metformin, include a current complete blood count (CBC) or vitamin B12 level
- 3. Current physical examination findings.
  - a. Include current blood pressure, weight, height
  - b. Report current diabetic foot exam (include visual inspection, vibration sensation assessed with a 128-Hz tuning fork, and either temperature or monofilament sensation)
- 4. Report of a dilated funduscopic examination obtained within the preceding 12 months.
- 5. Current ECG.
- 6. All pertinent clinical encounter notes related to the diagnosis and treatment of diabetes mellitus, including a recent note outlining degree of control/compliance and ongoing treatment plan.
- 7. FL4 with RTD and ALC status.
- 8. Any other pertinent information.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a Any changes in ASCVD risk factors
  - b. Current medications, doses, and adverse effects
- 2 Updated laboratory studies
  - a Current fasting blood glucose measurement and HbA1c level
  - b Current fasting CMP
  - c Current fasting lipid panel
  - d. Current quantitative spot urine albumin-to-creatinine measurement
  - e. If treatment includes metformin, include a current CBC or vitamin B12 level
- 3 Current physical examination findings.
  - a Include current blood pressure, weight, height
  - b. Report diabetic foot exam within the preceding 12 months (include visual inspection, vibration sensation assessed with a 128-Hz tuning fork, and either temperature or monofilament sensation)
- 4 Report of a dilated funduscopic examination obtained within the preceding 12-24 months
- 5 All pertinent interval clinical encounter notes related to the diagnosis and treatment of diabetes mellitus, including a recent note outlining degree of control/compliance and ongoing treatment plan.
- 6 Any other pertinent information.
- 7 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

### **III. Aeromedical Concerns**

Given that diabetes mellitus is a multi-systemic disease that also results in microvascular and macrovascular complications, the immediate and long-term aeromedical concerns are multiple. A primary concern is the risk for hypoglycemia in diabetics who require medication to control their blood glucose. Hypoglycemia is a frequent side effect of many anti-hyperglycemic agents, and risk varies with medication class. Symptoms of hypoglycemia include excess perspiration, tremulousness, nervousness or anxiety, dizziness and/or lightheadedness, central nervous system depression, confusion, difficulty speaking, and weakness. These symptoms are likely with moderate to severe hypoglycemia and are incompatible with flying duties. If hyperglycemia is prolonged, it can lead to polyuria, dehydration, nausea, fatigue, and changes in visual acuity. Subclinical hypoglycemia may result in subtle cognitive and performance decrements. The highest risk for serious consequences of hypoglycemia, including death, occurs in individuals with hypoglycemia unawareness. These individuals may not develop noticeable symptoms despite dangerously low blood glucose levels, and therefore they may not seek timely treatment. In addition to hypoglycemia, diabetes mellitus conveys an increased risk for atherosclerotic cardiovascular disease, including myocardial infarction and stroke. It is also associated with the development of microvascular and macrovascular

disease, including retinopathy, nephropathy, and neuropathy, which carry further aeromedical risks.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 65 individuals with an AMS containing the diagnosis of DM. Thirteen individuals (20%) were disqualified. A breakdown of the cases was follows: 0 FC I/IA cases, 29 FC II cases (9 disqualified), 29 FC III cases (4 disqualified), 7 ATC/GBC cases (0 disqualified), 0 MOD cases, and 2 RPA Pilot cases (0 disqualified).

| ICD-9 codes for Diabetes Mellitus |  |  |
|-----------------------------------|--|--|
| 250.00                            | Type 2 diabetes mellitus without mention of complication |  |
| 250.90                            | Type 2 diabetes mellitus with unspecified complications  |  |
| 250.01                            | Type 1 diabetes mellitus without mention of complication |  |
| 250.91                            | Type 1 diabetes mellitus with unspecified complications  |  |

| ICD-10 codes for Diabetes Mellitus |   |  |
|------------------------------------|---|--|
| E11.9                              | Type 2 diabetes mellitus without complications          |  |
| E11.8                              | Type 2 diabetes mellitus with unspecified complications |  |
| E10.9                              | Type 1 diabetes mellitus without complications          |  |
| E10.8                              | Type 1 diabetes mellitus with unspecified complications |  |

## IV. Suggested Readings

- 1. American Diabetes Association. *Standards of Medical Care in Diabetes* 2019. Diabetes Care 2018; 42(Suppl. 1): S1-S194. Complete text available at https://care.diabetesjournals.org/content/42/Supplement\_1. An abridged version of this article for primary care providers is available at https://clinical.diabetesjournals.org/content/37/1/11. A summary of annual revisions is available at https://care.diabetesjournals.org/content/42/Supplement\_1/S4.
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  AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/
  ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Jointly published in Circulation 2019; 139(25):e1046-e1081 and J Am Coll Cardiol 2019; 73(24):e285-e350. Erratum in: Circulation 2019; 139(25):e1178-e1181 and J Am Coll Cardiol 2019; 73(24):3237-3241. Available at https://www.ahajournals.org/doi/10.1161/CIR.0000000000000024.
- 3. American College of Cardiology ASCVD Risk Estimator Plus. Available at https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/.

### **WAIVER GUIDE**

Updated: Aug 2016

Supersedes Waiver Guide of Aug 2012

By: Capt Chris McLaughlin (RAM 17) and Dr Dan Van Syoc

Reviewed by: Col Pat Storms, Gastroenterology consultant to AF/SG

### **CONDITION:**

**Diverticular Disease of the Colon (Aug 2016)** 

### I. Waiver Consideration.

Diverticulitis or symptomatic diverticulosis is disqualifying for FC I/IA, FC II, FC III, and SWA duties. Before waiver consideration, aviators should have complete resolution of symptoms and be taking no medications incompatible with flying. For ATC duties, diverticular disease is not in and of itself a disqualifying condition, but any gastrointestinal hemorrhage, regardless of cause is disqualifying for FC I/IA, FC II, FC III, ATC, and SWA duties. For GBO duties, diverticular disease and gastrointestinal hemorrhage is not specifically disqualifying, but surgical colostomy and recurrent incapacitating abdominal pain of such nature to prevent satisfactory performance of duties is disqualifying for all classes.

Table 1: Waiver potential for colonic diverticular disease

| Flying Class (FC)               | Condition  | Waiver Potential<br>Waiver Authority# |
|---------------------------------|--|---------------------------------------|
| I/IA                            | History of symptomatic diverticulosis or diverticulitis, resolved+ | Yes<br>AETC                           |
|                                 | Symptomatic diverticulosis or diverticulitis                       | No<br>AETC                            |
| II and III, including untrained | History of symptomatic diverticulosis or diverticulitis, resolved+ | Yes<br>MAJCOM*                        |
|                                 | Symptomatic diverticulosis or diverticulitis                       | No<br>MAJCOM*                         |
| ATC/GBO/SWA                     | History of symptomatic diverticulosis or diverticulitis, resolved  | N/A                                   |

<sup>\*</sup>Waiver authority for untrained aviators is AETC

A review of AIMWTS through Jul 2016 showed 210 cases of diverticulitis. Breakdown was as follows: 2 FC I cases, 127 FC II cases (7 disqualified), 77 FC III cases (4

<sup>+</sup> Can consider indefinite waiver for untrained aviators with remote history of diverticular disease

<sup>#</sup> ACS evaluation at discretion of waiver authority

disqualified), 3 ATC/GBC cases, and 1 MOD case. Of the 11 disqualified members, 4 were for severe disease requiring surgical resection (3 FC II and 1 FC III), 1 was disqualified for multiple recurrent cases of diverticular disease (FC III) and the other 6 were primarily disqualified for other medical conditions.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for diverticular disease should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. Complete history of the problem to include all consultants seen, medications used and procedures, if any.
- C. Physical exam results.
- D. Labs evidence of no rectal bleeding; any colonoscopy results, if performed
- E. Gastroenterology or surgical consultation reports to include any imaging studies.
- F. Current treatment to include all medications and dates started.
- G. Detail of all other medical problems, if applicable.

The AMS for <u>waiver renewal</u> for diverticular disease should include the following:

- A. Updated history since last waiver
- B. Physical exam results.
- C. Labs any new labs, imaging tests and colonoscopy results since last waiver.
- D. Any pertinent consults and study results.
- E. Current treatment to include all medications and dates started.

### III. Overview.

Colonic diverticular disease is quite common, accounting for 300,000 hospitalizations and 1.5 million outpatient visits annually in the United States. It appears to be a condition unique to western developed countries, as it is nearly absent in rural Africa and Asia.<sup>2</sup> The left colon is involved in more than 90% of patients<sup>3</sup>, with transverse and ascending portions of the colon involved in decreasing order of frequency. Diverticular disease has less than a 5% incidence in persons less than age 40 but the incidence increases rapidly thereafter, with about 60% of the general population developing the condition by age 80. The true incidence is difficult to ascertain as most patients are asymtomatic<sup>4, 5</sup>, but recent studies suggest an increasing prevalence of diverticular disease, especially in patients under the age of 50.6 Low dietary fiber intake, elevated BMI and physical inactivity are traditionally linked to the development of diverticulosis<sup>7</sup>, but a 2012 study with 2104 participants actually demonstrated an inverse correlation, in that a high fiber diet and more frequent bowel movements were associated with an increased rather than decreased prevalence of asymptomatic colonic diverticulosis.<sup>8</sup> Further, their data did not demonstrate any association between fat, red meat, or physical activity and the presence of diverticulosis. In an accompanying editorial, it was noted that there have been large

studies demonstrating an association between low fiber intake and diverticular complications, whereas the cited study focused on asymptomatic diverticulosis.<sup>9</sup>

The pathogenesis of diverticular disease is unknown, but is thought to reflect an interplay of anatomical factors in conjunction with increased intraluminal pressure, resulting in herniations of the colonic mucosa and submucosa through the colonic muscular layer. <sup>10</sup> Technically, these lesions are actually pseudodiverticula because all layers of the colon are not involved. 11 Diverticulosis is thought to be asymptomatic in 80% of individuals, and the remaining 20% can be divided into two categories: symptomatic diverticulosis and diverticulitis. <sup>12</sup> Symptomatic diverticulosis is characterized by episodic pain, altered bowel habits and a lack of inflammation, and may mimic symptoms produced by irritable bowel syndrome. The diagnostic approach to patients with abdominal pain and altered bowel function generally includes colonoscopy in order to assess for significant mucosal pathology. Traditional medical treatment includes a high-fiber diet consisting of wheat bran and/or commercial bulking agents, but research findings bring these recommendations into question. A systematic review of 11 studies that investigated probiotics as a treatment for symptomatic diverticulosis found that the quality of studies and strength of evidence lacked sufficient weight to recommend for or against their use.<sup>13</sup> Antispasmodics such as dicyclomine (Bentyl®) can bring symptomatic relief in patients with cramping discomfort due to diverticulosis, but narcotic analgesics should be avoided.

Patients with diverticulitis often present with left lower quadrant pain and tenderness, nausea, fever, and leukocytosis. Plain abdominal films can identify free air in the abdomen indicative of perforation, but a CT scan with oral and intravenous contrast is the preferred imaging modality for confirming the diagnosis. Treatment is based on the overall health of the patient and the severity of the disease. Stable, uncomplicated patients who tolerate liquids can be treated as outpatients with oral antibiotics. The success rate of such conservative treatment in patients with acute uncomplicated diverticulitis is greater than 90 percent. There is growing discussion regarding the value of antibiotics in treatment of uncomplicated diverticulitis, but the evidence is not strong enough to recommend against treating with antibiotics. 1, 14, 15, 16 Older patients, those with comorbid conditions, and anyone unable to tolerate oral fluids should be hospitalized with IV antibiotics and fluids. Those with complications such as perforation, abscess formation, fistulization, sepsis or partial obstruction should be hospitalized for medical and/or surgical treatment. About 10% of hospitalized patients require surgical treatment.

After the first episode of acute diverticulitis, approximately 25% of medically-treated cases will experience a recurrence.<sup>5</sup> With each additional recurrence, the risk of further recurrence and complications increases. Physicians have historically stressed the avoidance of nuts, seeds and popcorn to reduce the risk of recurrent diverticulitis. Some recent studies have refuted this notion as a cause of diverticular complications, and these dietary restrictions should no longer be routinely recommended.<sup>17</sup> Historically, surgical resection of the affected colon was recommended after the second uncomplicated episode of acute diverticulitis in those over age 50 and after the first episode in those under age 50. This was based on studies showing younger patients with more virulent disease and a greater overall risk of recurrence due to a longer lifespan. However, new data has

questioned these assumptions and the decision to perform an elective colectomy should be determined based on each patient's own set of circumstances and treatment preference. Such patients should be counseled on the risks and benefits of accepting or declining elective segmental-colectomy for diverticular disease as several studies have shown that up to 25% of patients experienced persistent symptoms after elective surgery. <sup>18, 19</sup>

Acute diverticular hemorrhage can be dramatic and can lead to acute incapacitation and hemorrhagic shock. In left-sided colonic diverticulosis, this bleeding is often seen as bright red blood per rectum. Slower rates of bleeding or bleeding from the more proximal colon may result in darker blood or clots in the stool. The mechanism for diverticular hemorrhage is poorly understood, but the bleeding is arterial in nature and is thought to relate to endothelial damage. Bleeding stops spontaneously in up to 90% of cases but can recur during the index hospitalization, or post discharge in up to 38% of patients. Current treatment has shifted from angiography and urgent surgery to mechanical colonoscopic interventions.<sup>20</sup>

#### IV. Aeromedical Concerns.

Acute diverticular hemorrhage or perforation are capable of causing in-flight physical incapacitation, but altered bowel habits, abdominal distention, episodic pain, nausea, and flatulence related to symptomatic diverticulosis could be a distraction and affect crew availability. An aviator with acute diverticulitis would be ill-suited to fly due to fever and pain. Once resolved and stable without residual symptoms, returning the pilot to flying duties should not present a hazard to flying safety, the individual's health, or mission completion.<sup>21</sup>

| ICD-9 code for | diverticular disease |
|----------------|----------------------|
| 562.1          | Diverticula of colon |

| ICD-10 code for diverticular disease |   |
|--------------------------------------|---|
| K57.30                               | Diverticulosis of large intestine without |
|                                      | perforation or abscess without bleeding   |

## V. References.

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- 11. Prather, C. Inflammatory and Anatomic Diseases of the Intestine, Peritoneum, Mesentery, and Omentum. Ch. 144 in *Goldman's Cecil Medicine*, 24<sup>th</sup> ed., Saunders, 2011.
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# Dry Eye Syndrome (Keratoconjunctivitis Sicca) (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** None since last review. Grading is <u>post-treatment</u> when considering waiver potential. MSD C24.

#### I. Waiver Consideration

Dry eye is disqualifying for Flying Class I, IA, II, III, and SWA duties. Quality of vision can easily be compromised with chronic dry eye syndrome, so visual acuity standards apply. Generally, Grade 1 Dry Eye Syndrome does not require waiver action as it is easily controlled by lid hygiene and occasional use of artificial tears. Grade II and III dry eyes would require waiver action if only controlled with artificial tears, topical medications, or punctual plugs. Grade IV Dry Eye Syndrome would generally not be waiverable on maximal medical therapy. There is no disqualification for ATC, GBO, or OSF personnel with Dry Eye Syndrome. However, if the dry eye affects visual acuity to a level that the member cannot meet vision standards, then that is disqualifying. Dry Eye Syndrome is not disqualifying for retention.

**Table 1: Waiver potential for Dry Eve Syndrome** 

| Flying Class (FC) | Waiver Potential   | ACS Review/Evaluation  |
|-------------------|--|------------------------|
|                   | Waiver Authority   |                        |
| FC I/IA           | Yes – Grade 1 only (may not be considered disqualifying) | At the request of AETC |
|                   | No – Grade 2 or worse on tears for at                    |                        |
|                   | least 3 months   |                        |
|                   | AETC   |                        |
| FC II/III         | Yes – Grade 2 and 3                                      | At the request of the  |
| SWA               | No – Grade 4 on treatment (tears,                        | MAJCOM                 |
|                   | Restasis®, Xiidra®)                                      |                        |
|                   | MAJCOM   |                        |
| ATC/GBO/OSF       | N/A  | N/A                    |

AIMWTS review in Jun 2018 revealed a total of 96 cases submitted for waiver consideration with the diagnosis of dry eye with 84 cases approved for waiver. Breakdown of the cases revealed 7 FC I/IA cases (1 disqualification), 44 FC II cases (4 disqualifications), 7 RPA cases (1 disqualification), 33 FC III cases (4 disqualifications), and 7 ATC/GBC cases (1 disqualifications).

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

# A. <u>Initial Waiver Request:</u>

- 1. List and fully discuss all clinical diagnoses requiring a waiver.
- 2. History history of all dry eye symptoms; any underlying causative factors, all treatments attempted and effectiveness of the therapy (medical and surgical), and any impact on job/daily life. History of contact lens use, including length and pattern of wear must be included in history. Specific description of medical interventions tried, and current treatment regimen if applicable.
- 3. Physical full eye exam to include visual acuity measurement, an external examination, and slit-lamp examination. In addition, include results of the tear film break-up time, ocular surface dye testing, and the Schirmer test.
- 4. Ophthalmology consultation report (cornea specialist preferred).
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

Interval AMS with particular attention to clinical changes on Ophthalmologist Consultation.

## **III. Aeromedical Concerns**

The aeromedical issues relate to the subjective annoyance of dry eye symptoms and also with visual performance decrements. In more severe cases individuals can have significant visual impairment and should not participate in military aviation duties. The dry air of most cockpits will exacerbate symptoms in most affected airmen. The increase in use of contact lens among aircrew has significantly increased the incidence of dry eyes, and it is vitally important that new dry eye medications are not inappropriately used to treat contact lens intolerance or contact lens related dry eyes. Most artificial tear drops are safe in the aviation environment, as are punctal plugs if declared stable by the treating ophthalmologist.

An attempt to grade severity of dry eye symptoms is depicted in Table 2. The results of this grading scheme may drive the level of treatment. However, symptoms of dry eye syndrome do not necessarily reflect the severity of the disease. The lack of concordance between signs and symptoms presents a problem not only in the diagnosis but also in the construction of a treatment plan and when designing adequate clinical trials.<sup>2</sup>

**Table 2: Dry Eye Disease Severity Grading Scheme** 

| Dry Eye Severity level  | <u> </u>         | 2                | 3                 | 4                |
|-------------------------|------------------|------------------|-------------------|------------------|
| Discomfort, severity,   | Mild and/or      | Moderate,        | Severe,           | Severe and/or    |
| and frequency           | episodic; occurs | episodic, or     | frequent, or      | disabling and    |
|                         | under            | chronic; stress  | constant          | constant         |
|                         | environmental    | or no stress     | without stress    |                  |
|                         | stress           |                  |                   |                  |
| Visual Symptoms         | None or          | Annoying         | Annoying,         | Constant and/or  |
|                         | episodic mild    | and/or activity- | chronic,          | possibly         |
|                         | fatigue          | limiting,        | constant          | disabling        |
|                         |                  | episodic         | limiting activity |                  |
| Conjunctival injection  | None to mild     | None to mild     | Mild              | Moderate to      |
|                         |                  |                  |                   | Severe           |
| Conjunctival staining   | None to mild     | Variable         | Mild to           | Marked           |
|                         |                  |                  | Moderate          |                  |
| Corneal                 | None to mild     | Variable         | Marked central    | Severe           |
| staining(severity/      |                  |                  |                   | punctuate        |
| location)               |                  |                  |                   | erosions         |
| Corneal tear signs      | None to mild     | Mild debris,     | Filamentary       | Filamentary      |
|                         |                  | decreased        | keratitis, mucus  | keratitis, mucus |
|                         |                  | meniscus         | clumping,         | clumping, ↑ tear |
|                         |                  |                  | increased tear    | debris,          |
|                         |                  |                  | debris            | ulceration       |
| Lid/Meibomian           | MGD variably     | MGD variably     | Frequent          | Trichiasis,      |
| glands                  | present          | present          |                   | keratinization,  |
|                         |                  |                  |                   | symblepharon     |
| TBUT (seconds)          | Variable         | <u>≤</u> 10      | <u>≤</u> 5        | Immediate        |
| Schirmer score (mm      | Variable         | <u>≤</u> 10      | <u>≤</u> 5        | <u>≤</u> 2       |
| tears/5 minutes)        |                  |                  |                   |                  |
| MGD = Meibomian gland d | isease           |                  | ·                 |                  |

MGD = Meibomian gland disease

TBUT = tear film break-up time

| ICD-9 code for | · Dry Eye Syndrome |
|----------------|--------------------|
| 375.15         | Dry eye syndrome   |

| ICD-10 code for Dry Eye Syndrome |                                    |
|----------------------------------|------------------------------------|
| H04.12                           | Dry eye syndrome of lacrimal gland |

# **IV. Suggested Readings**

- 1. Galor A, Feuer W, Lee DJ, et al. Prevalence and Risk Factors of Dry Eye Syndrome in a United States Veterans Affairs Population. Am J Ophthalmol, 2011, 152(3), 377-84.
- 2. Lemp MA. Advances in Understanding and Managing Dry Eye Disease. Am J Ophthalmol, 2008; 146: 350-56.

## Dysmenorrhea (Feb 2019)

Reviewed: Dr. Hattie McAviney (RAM 20), Dr. Dan Van Syoc (Deputy Chief, ACS), Lt Col Jason Massengill (AF/SG consultant for OB/GYN), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Format

#### I. Waiver Consideration

Dysmenorrhea is disqualifying for retention, as well as for all flying classes when symptoms result in an inability to perform duties, cause frequent absences from duty or require ongoing specialty f/u more than annually. It is also disqualifying for FC I/IA, II, III, and SWA personnel when it results in other disqualifying conditions (e.g., anemia, osteoporosis, etc.). Most medications used to prevent or treat dysmenorrhea are compatible with flying duties. Hormonal contraceptives and the acute use of several NSAIDs (e.g., ibuprofen, naproxen, aspirin, etc.) are approved for flying/operational duties and do not require waiver as long as the underlying condition is not interfering with the satisfactory job performance.

Table 1: Waiver potential for dysmenorrhea

| Flying Class<br>(FC)   | Condition <sup>1</sup>  | Waiver<br>Potential<br>Waiver<br>Authority | ACS<br>Review/Evaluation |
|------------------------|---|--|--------------------------|
| I/IA                   | Primary dysmenorrhea<br>controlled with NSAIDs<br>(ibuprofen, naproxen,<br>aspirin) and/or hormonal<br>contraceptives | N/A  | No                       |
|                        | Primary dysmenorrhea not controlled on approved NSAIDs and/or hormonal contraceptives                                 | No<br>AETC                                 | No                       |
| II, III<br>ATC/GBO/SWA | Primary dysmenorrhea<br>controlled with NSAIDs<br>and/or hormonal<br>contraceptives                                   | N/A  | No                       |
|                        | Primary dysmenorrhea not controlled on approved NSAIDs and/or hormonal contraceptives                                 | Maybe <sup>2</sup><br>AFMRA                | No                       |

<sup>1.</sup> For dysmenorrhea resulting from secondary causes see waiver guides for Endometriosis, Uterine Fibroid and Pelvic Inflammatory Disease.

<sup>2.</sup> Waiver in untrained personnel is unlikely; waiver authority for such cases is AFMRA.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

# A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment. History should include the following: age of menarche, onset of pain, relation with onset of menstrual flow, severity, location of pain, additional symptoms, impact on activities, presence of pain not related to menses, prior medical and surgical treatment and effectiveness.
- 2. Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated).
- 3. Documentation of a pelvic examination.
- 4. Gynecologic consultation reports, if NSAIDs and/or hormonal contraceptives do not control pain or if abnormal pelvic exam.
- 5. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 6. Current physical examination findings.
- 7. FL4 with RTD and ALC status, if member did not meet retention status.
- 8. Any other pertinent information.
- 9. The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

## B. Renewal Waiver Request:

- 1 Interval history since last waiver submission.
- 2 Pelvic examination.
- 3 Consultation report from the treating physician.
- 4 The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

#### **III. Aeromedical Concerns**

Symptoms of primary dysmenorrhea are typically time-predictable and time-limited, and are often well-controlled with aeromedically approved medications. In these cases, it is not expected to be acutely incapacitating and continued flying should not be problematic. In some cases though, primary dysmenorrhea can cause menstrual pains severe enough to distract or even incapacitate. Potential accompanying symptoms of nausea, vomiting, diarrhea, headaches, dizziness or low back pain may also be distracting in flight and could adversely affect mission safety and completion. For these reasons, if symptoms are not controlled or require non-approved medications, then primary dysmenorrhea is disqualifying for all flying classes.

A review of AIMWTS through Nov 2018 revealed 19 aviators with a diagnosis of dysmenorrhea. There was 1 FC I/IA case (no disqualification), 1 FC II case (no

disqualification), 12 FC III cases (2 disqualified), 2 ATC/GBC cases (no disqualifications), and 3 MOD cases (no disqualifications). The two disqualified cases were due to intractable pelvic pain.

| ICD-9 codes for Dysmenorrhea |              |
|------------------------------|--------------|
| 625.3                        | Dysmenorrhea |

| ICD-10 codes for Dysmenorrhea |                           |
|-------------------------------|---------------------------|
| N94.4                         | Primary dysmenorrhea      |
| N94.5                         | Secondary dysmenorrhea    |
| N94.6                         | Dysmenorrhea, unspecified |

# **IV. Suggested Readings**

- 1. Burnett M and Lemyre M. No. 345-Primary Dysmenorrhea Consensus Guideline. Journal of Obstetrics and Gynaecology Canada. 2017; 39(7):585-595. DOI: https://doi.org/10.1016/j.jogc.2016.12.023
- 2. Gorbandt MB and Knittig RA. Women's Health Issues in Aerospace Medicine. In Davis JR, Johnson R, Stepanek J, eds. *Fundamentals of Aerospace Medicine*, 4<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2008:480-490.
- 3. Osayande AS and Mehulic S. Diagnosis and Initial Management of Dysmenorrhea. Am Fam Physician. 2014; 89(5):341-346.
- 4. Smith RP and Kaunitz AM. Primary dysmenorrhea in adult women: Clinical features and diagnosis. UpToDate. Online version 22.0. Mar 2018.
- 5. Smith RP and Kaunitz AM. Treatment of primary dysmenorrhea in adult women. UpToDate. Online version 35.0. Mar 2018.

#### **WAIVER GUIDE**

Updated: Jan 2016

Supersedes Waiver Guide of Oct 2011

By: Col Elizabeth Anderson-Doze (RAM 16), Neuropsychiatry branch staff & Dr. Dan

Van Syoc

## **CONDITION:**

**Eating Disorders (Jan 2016)** 

## I. Waiver Consideration.

Eating disorders are disqualifying for all flying classes to include ATC/GBO and SWA duties, and may be disqualifying for continued service. Untreated or undertreated eating disorders may have potentially disastrous consequences. If the diagnostic criteria are met for anorexia nervosa, bulimia nervosa, binge-eating disorder, other specified feeding or eating disorder, or unspecified feeding or eating disorder, the aviator is disqualified.

To be considered for waiver, a mental health evaluation with accurate diagnosis per the DSM-5 is the vital first step. USAF psychologists/psychiatrists familiar with aeromedical standards are the preferred choice for evaluation and potential development of the treatment plan.

Table 1: Waiver potential for eating disorders.

| Flying Class (FC)               | Waiver Potential<br>Waiver Authority | Waiting Period<br>Post-Treatment |
|---------------------------------|--------------------------------------|----------------------------------|
| I/IA                            | Maybe<br>AETC                        | > 2 year <sup>1,2</sup>          |
| II,III, and RPA Pilot untrained | Yes<br>MAJCOM                        | > 2 year <sup>1,2</sup>          |
| II/III<br>ATC/GBO/SWA           | Yes<br>MAJCOM                        | > 1 year <sup>2,3</sup>          |

<sup>1</sup> For all UNTRAINED individuals (FC I/IA, II/III, or ATC/GBO/SWA) with a history of eating disorders, a minimum of two years remission with successful treatment must be documented.

NOTE: Recommend that initial waiver be granted for only one year due to the high rate of relapse. Do NOT recommend an indefinite waiver.

A review of the AIMWTS database through Jan 2016 revealed 48 cases of eating disorders. Of the 48 cases, 31 (65%) were disqualified. Breakdown of the cases revealed: 5 FC I/IA cases (3 disqualifications), 5 FC II cases (3 disqualifications), 23 FC III cases (16 disqualifications), 3 MOD cases (1 disqualification), and 12 ATC/GBC cases (8 disqualifications). Of the 31 disqualified, 20 had a history of bulimia, 4 with anorexia nervosa and 7 with eating disorder unspecified or other specified.

<sup>2</sup> Patients with eating disorders must meet minimum aviation weight standards

<sup>3</sup> For TRAINED individuals (FC II, FC III, or ATC/GBO/SWA) with a history of eating disorders a minimum of one year remission with successful treatment must be documented.

# II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

AFI 48-123 –Chapter 6, USAF Medical Standards Directory, Section Q, and the Aeromedical Consultation Service (ACS) Waiver Guide addresses waiver evaluations Step 1 - Is the aviator ready for waiver submission?

| fur<br>(N            | waiver is submitted when the member is asymptomatic (back to best baseline actioning), as applicable to diagnostic category, for the specified time-frame below ote: medications/psychotherapy for optimal therapeutic benefit are permissible d often advisable after initial symptom resolution): |
|----------------------|---|
|                      | 1 Year—Eating Disorders, Psychotic Disorders & Somatic Symptom and Related Disorders  |
|                      | be considered for an aeromedical waiver, any disqualifying condition must meet following criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg. 31):   |
|                      | Not pose a risk of sudden incapacitation  |
| Ш                    | Pose minimal potential for subtle performance decrement, particularly with regard to the higher senses  |
|                      | Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment  |
|                      | If the possibility of progression or recurrence exists, the first symptoms or signs must be easily detectable and not pose a risk to the individual or the safety of others   |
|                      | Cannot require exotic tests, regular invasive procedures, or frequent absences to   |
|                      | monitor for stability or progression  Must be compatible with the performance of sustained flying operations  |
| obtain N<br>Instruct | Before beginning the Aeromedical Summary (AMS), Flight Surgeon must<br>Mental Health consultation and ensure it contains items specified below:<br>ions for the Mental Health Provider  |
| The men              | ntal health evaluation must include a <u>comprehensive written report</u> addressing:<br>Consultation must address each criteria in Step 1B   |
|                      | Clinical mental health history (description of symptoms, treatment modality, frequency and compliance with treatment, relevant personal and family history, and perceived impact on occupational duties)  |
|                      | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)   |
|                      | Appropriate laboratory results (i.e., thyroid, liver function tests, drug screen, CDT**, chemical profile) ** for alcohol cases, please comment on Carbohydrate-Deficient Transferrin (CDT results**  |
|                      | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental illness)   |
|                      | Current and past aviation related duties and any history of current and past occupational performance difficulties (to include perceived impact of mental health condition on performance of duties)  |

|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep   |
|----------|--|
|          | Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-III, PAI, or similar personality test, as well as cognitive testing/screening). Current mental status   |
|          | Diagnosis  |
|          | Motivation to fly or engage in special duty operations (past and current)  |
|          | Recommendation for future psychological and medical treatment  |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)   |
|          | Please forward copies of all mental health or behavioral health records (Mental health, Behavioral Health, civilian provider, ADAPT, FAP, and/or inpatient treatment records) including the raw scores, standard scores, and in some cases T-scores from completed psychological or neuropsychological testing, in addition to the written report to ACS Neuropsychiatry Branch (address is below) when member completes the attached Release of Information form (information will be reviewed by ACS Clinical Psychologist)  |
| Step 3 - | Items for the Flight Surgeon to include in the AMS:  |
|          | AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safe  |
|          | Summarize Mental Health history and focus on occupational impact  ** If 2 or more months have passed since the comprehensive evaluation/report was completed,  |
|          | the flight surgeon should address how the member has done since and consult with the mental health provider if the member has been seen at mental health since the evaluation**  Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)  Appropriate laboratory results (i.e., thyroid, liver function tests, drug screen, CDT**, chemical profile)  ** for alcohol cases, please comment on Carbohydrate-Deficient Transferrin (CDT) results**  Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if possible - please address current state of any triggers for the mental illness)  Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep |
|          | Current mental status  |
|          | Diagnosis  Mativation to flat (next and assurant)  |
|          | Motivation to fly (past and current)   |
|          | Recommendation for future psychological and medical treatment  Progressis (actimate of symptom resources), potential impact on future sylvation related dytics)  |
| <br>C4 4 | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)   |
| Step 4 - | Additional items to complete the waiver package:  Letter of support from command  NOTE:  |
|          | Have member complete/sign a Release of Information f SUBSTITUTE FOR MENTAL HEALTH Clinic (where treatment was provided) for processing. Instruct the MHC to release copies of MH record (provide MHC with ACS Neuropsychiatry Branch contact information, if necessary) and send to:   |
|          | ACS Agrospage Medicine Branch IISAESAM/FECA  |

ACS Aerospace Medicine Branch, USAFSAM/FECA c/o Neuropsychiatry Branch

# 2510 Fifth Street Bldg 840 Wright Patterson AFB, OH 45433-7913 Fax: (937) 904-8753 DSN: 674-8753

Please feel free to contact the ACS Neuropsychiatry Branch with questions:

Mr. John Heaton: DSN 798-2766

john.heaton.7@us.af.mil

## AUTHORIZATION FOR DISCLOSURE OF MEDICAL OR DENTAL INFORMATION

#### PRIVACY ACT STATEMENT

In accordance with the Privacy Act of 1974 (Public Law 93-579), the notice informs you of the purpose of the form and how

it will be used. Please read it carefully.

AUTHORITY: Public Law 104-191; E.O. 9397 (SSAN); DoD 6025.18-R.

PRINCIPAL PURPOSE(S): This form is to provide the Military Treatment Facility/Dental Treatment Facility/TRICARE Health Plan

with a means to request the use and/or disclosure of an individual's protected health information.

ROUTINE USE(S): To any third party or the individual upon authorization for the disclosure from the individual for: personal

use; insurance; continued medical care; school; legal; retirement/separation; or other reasons.

DISCLOSURE: Voluntary. Failure to sign the authorization form will result in the non-release of the protected health information.

This form will not be used for the authorization to disclose alcohol or drug abuse patient information from medical records or for authorization to disclose information from records of an alcohol or drug abuse treatment program. In addition, any use as

| disclose psychotherapy r  | or disclose psychotherapy notes may no<br>notes.   | ot be combined with and   | ner autn  | orization ex   | ccept one to use or   |
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| 1. NAME (Last, First, Midd.   | le Initial)  | 2. DATE OF BIRTH (YY  | YMMDD)  | 3. SOCIAL  | SECURITY NUMBER   |
| 4. PERIOD OF TREATME  | NT: FROM - TO (YYYYMMDD)   | 5. TYPE OF TREATMEN   | 「(X one)  |  |   |
|   | ALL  | OUTPATIENT  | INPATI  | FNT [  | вотн  |
|   | SECTION II -   | DISCLOSURE  | 1002310   |  | ВОТП  |
| 6. I AUTHORIZE  | 323,000  |   | RELEASI   | EMYPATIEN  | TINFORMATION TO:  |
|   | (Name of Facility/TRICARE Health F   |   | SPECIAL PROPERTY OF SPECIAL PROPERTY.   | A STORY OF COMMENT OF  |   |
|   | ACILITY, OR TRICARE HÉALTH PLAN Aeromedical Consultation Service Medicine  | b. ADDRESS (Street, City, 2510 5th Street, Bldg 840, Patterson AFB, OH 45433  | Area B W  |  |   |
|   |  |   |   |  |   |
| c. TELEPHONE (Include Ar  | Sec. And desired Sec. and description of the control of the contro | d. FAX (Include Area Code   | / (937) 9   | 904-8753   |   |
| PERSONAL USE INSURANCE 8. INFORMATION TO BE RE All Mental/Behavioral Head to include, but not limited to  | CONTINUED MEDICAL CARE RETIREMENT/SEPARATION  LEASED Ith (Sections A-F), ADAPT, FAP, and/or civi or background questionnaires, intake forms, partient records, treatment notes (not AHLTA or continued).   | OTHER (Specify) AERON SCHOOL WAIVE  | R PACKA<br>e). Please   | include any  | and all of the records  |
| 9. AUTHORIZATION STA  |  | (C) - |   |  |   |
| 9. AUTHORIZATION STA  | DATE (YYYY)  |   |   | □ ACT  | ON COMPLETED  |
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| where my medical record TRICARE Health Plan raname will have used and b. If I authorize my protoprivacy protection regulars. I have a right to insport with the requirements of d. The Military Health South the TRICARE Health obtain this authorization. I request and authorize to the named individual/ | he named provider/treatment facility/TR<br>organization indicated.   | ter if this is an authorizate that if I later revoke this on the basis of this author to someone who is not edisclosed and would not ested health information ons found in the Privacy ealth Plan) may not control on Plan or eligibility for TRECARE Health Plan to re   | ion for in authoriza orization trequired longer be to be use Act and dition treatlicaRE H | formation pation, the period of disclosed or disclosed of the following period | possessed by the erson(s) I herein with federal sed, in accordance 64.524. MTFs/DTFs, payme benefits on failure |
| 11. SIGNATURE OF PATIEN   | T/PARENT/LEGAL REPRESENTATIVE  | 12. RELATIONSHIP TO PA<br>(If applicable)<br>self   | ΠΕΝΤ  | 13. DAT  | <b>E</b> (YYYYMMDD)   |
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| AUTHORIZATION REVOKED   | 15. REVOCATION COMPLETED BY  |   |   | 16. DAT  | E (YYYYMMDD)  |
| 17. IMPRINT OF PATIENT IS   | DENTIFICATION PLATE WHEN AVAILABLE   | SPONSOR NAME: SPONSOR RANK: FMP/SPONSOR SSN: BRANCH OF SERVICE: PHONE NUMBER:   |   |  |   |

- D. Psychiatric evaluation and treatment summary by a doctoral level provider. The evaluation should include objective psychological testing of the person's emotional and The AMS for an <u>initial waiver</u> for eating disorders should include the following:
- A. History Address pertinent positives and negatives such as symptoms of amenorrhea, constipation, abdominal pain, cold intolerance, lethargy and excess energy (activity level), and any social, occupational, administrative or legal problems associated with the case. Comment regarding stability of patient's weight.
- B. Physical height and weight, blood pressure, skin, cardiovascular, abdominal and neurologic.
- C. Lab work including: complete blood count (CBC), chemistry 16 (electrolytes, glucose, calcium, magnesium, phosphorous, blood urea nitrogen, and creatinine), urinalysis, and ECG.
- D. Psychiatric evaluation and treatment summary by a doctoral level provider. The evaluation should include objective psychological testing of the person's emotional and cognitive disposition, such as the most recent edition of the Minnesota Multiphasic Personality Inventory (MMPI) and the Wechsler Adult Intelligence Scales, fourth edition (WAIS-IV).
- E. Dental evaluation for bulimia nervosa and others that purge.
- F. Medical evaluation board (MEB) reports if applicable.
- G. Input from the individual's commander/supervisor regarding the aviator's current status.

The AMS for a <u>renewal waiver</u> should include the following:

- A. History assessment for recurrences. Comment regarding stability of patient's weight.
- B. Physical exam: height and weight, blood pressure, skin, cardiovascular, abdominal, and neurologic.
- C. Psychiatric evaluation for first renewal and if clinically indicated on subsequent renewals.

## III. Overview.

#### **Basic Features**

Eating disorders are characterized by a persistent disturbance of eating behavior resulting in altered consumption or absorption of food that impairs health or psychosocial functioning. Five adult eating disorder diagnoses are recognized in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5): anorexia nervosa, bulimia nervosa, binge-eating disorder, other specified feeding or eating disorder, and unspecified feeding or eating disorder. Comorbidity with a wide range of other mental health disorders (e.g., substance use disorders, mood disorders, anxiety disorders) is common in eating disorders. The average age of onset is 18 years, but patients may present from late childhood through adulthood.<sup>2</sup>

# Anorexia Nervosa

Food restriction leading to significantly low body weight, intense fear of gaining weight with corresponding behavior that interferes with weight gain, and cognitive distortions about one's weight are the three essential features of anorexia nervosa. Multiple medical

conditions, such as hypotension, hypothermia, and bradycardia are associated with anorexia nervosa due to the semi-starvation and purging behaviors. Less than 50% of anorexics recover within 10 years, 25% become chronic, and mortality can be as high as 25%. Completed suicides are a documented consequence of anorexia nervosa and can reach rates of 12 per 100,000. Prevalence is much higher in females than males (10 to 1) with a 12-month prevalence of approximately 0.4% in young females.

## **Bulimia Nervosa**

Similar to anorexia nervosa, bulimia nervosa has three prominent features - recurrent episodes of binge eating, utilizing inappropriate behaviors (e.g., self-induced vomiting, laxatives, excessive exercise) to avoid gaining weight, and excessively emphasizing one's body in self-evaluation. Laboratory abnormalities are common as a result of the purging behavior and have been linked to hypokalemia which can provoke arrhythmias, and hyponatremia, which increases the risk of seizures. Twelve month prevalence in young females is 1-1.5%. Prognosis for bulimics is better than anorexics. However, fewer than 70% recover within 10 years, while 30% continue to binge eat and purge.

# **Binge-Eating Disorder**

Recurrent episodes of consuming an abnormally large amount of food combined with a sense of helplessness to control one's eating behavior are the defining characteristics of binge-eating disorder. The episodes occur weekly for at least three months and the binge-eating is not followed by inappropriate methods of weight loss. Binge-eating disorder is more common in men than the aforementioned eating disorders, with females twice as likely as males to have the disorder (prevalence of 1.6% and 0.8% respectively).<sup>1</sup>

## **Other Specified Feeding or Eating Disorder**

This diagnosis is used when the symptoms present cause significant distress or functional impairment but do not meet full criteria for the other eating disorders. DSM-5 gives guidance on possible cases, such as Atypical Anorexia Nervosa and Purging Disorder.<sup>1</sup>

## **Unspecified Feeding or Eating Disorder**

Similar to Other Specified Eating Disorder, this category is used when clinically significant symptoms are present that do not meet full criteria for one of the other eating disorders. It is useful for situations in which the clinician does not have sufficient information for a more specific diagnosis.<sup>1</sup>

## **Treatment Options**

Common treatment options include education on eating disorders and how they may manifest in a particular person's life, lifestyle changes, psychotherapy, and medications. Medications are typically recommended only if other measures are not effective and are generally less helpful in eating disorders as compared to other psychiatric conditions. They are often more helpful with co-occurring psychiatric illness than the eating disorder.

Healthy lifestyle interventions (exercise, relaxation, deep breathing, meditation, bibliotherapy, healthy eating, meaningful social connections, etc.) should always be considered in treatment planning.

## IV. Aeromedical Concerns.

A significant concern is the comorbidity of physical and emotional difficulties that lower the person's stamina for managing the high stress of military flying. For example, eating disorders can cause life-threatening metabolic alkalosis, hypokalemia, seizures, dehydration, and hypotension which impact readiness, mission completion, and flying safety. Anxiety and depression are comorbidities highly associated with eating disorders, and there exists an increased risk of suicide. Another area of concern is the strong association between eating disorders and personality disorders. Problematic personality characteristics common in eating disorders, such as emotional reactivity and perfectionism, may interfere with crew resource management and other aspects of crew relations essential to successful flying. Further, the course and outcome of these disorders is highly variable and marked by relapse with periods of remission alternating with recurrences.

| ICD-9/ICD-10 codes for eating disorders |  |  |
|---|--|--|
| 307.1/F50.01/.02                        | Anorexia nervosa                           |  |
| 307.51/F50.2                            | Bulimia nervosa                            |  |
| 307.51/F50.8                            | Binge-eating disorder                      |  |
| 307.59/F50.8                            | Other specified feeding or eating disorder |  |
| 307.50/F50.9                            | Unspecified feeding or eating disorder     |  |

#### V. References.

- 1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. American Psychiatric Publishing, Arlington, VA, 2013.
- 2. Hudson JI, Hiripi E, Pope HG Jr, and Kessler RC. The Prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. Biol Psychiatry, 2007; 61: 348-58.
- 3. Bergh C, Brodin U, Lindberg G, and Södersten P. Randomized controlled trial of a treatment for anorexia and bulimia nervosa. Proc Natl Acad Sci USA, 2002; 99(14): 9486-91.
- 4. Keel PK, Mitchell JE, Miller KB, et al. Long-term Outcome of Bulimia Nervosa. Arch Gen Psychiatry, 1999; 56: 63-69.
- 5. Herzog, David B.; Keller, Martin B.; Lavori, Philip W.; Kenny, Gina M.; Sacks, N. R. The prevalence of personality disorders in 210 women with eating disorders. Journal of Clinical Psychiatry, Vol 53(5), May 1992, 147-152.
- 6. Lilenfeld, R. R., Wonderlich, S., Riso, L. P., Crosby, R. & Mitchell, J. Eating disorders and personality: a methodological and empirical review. Clinical Psychology Review, 2006; 26, 3: 299-320.

# ECG Findings in USAF Aircrew, Disposition of (Jan 2019)

The following guidelines standardize the aeromedical evaluation and recommendations for 12-lead electrocardiographic (ECG) findings of individuals who must qualify for any class of flying duties. One goal is to streamline the local evaluation and minimize testing and travel to the Aeromedical Consultation Service (ACS). Aircrew with normal or normal variant ECG findings **as reviewed by the ECG Library** require no further evaluation or follow-up and no waiver action. Additional local studies or an ACS evaluation may be requested by the ECG Library on all individuals with borderline or abnormal ECG findings which are new or not previously evaluated. Originals of all ECGs and any other cardiovascular studies (even if normal) must be forwarded to the ECG library for review and image storage per AFI.

If additional studies are performed at the local level and reviewed through the ECG Library as normal or normal variant, no further workup is needed. If the additional studies are reviewed as borderline or abnormal, further evaluation will be directed through the ECG Library. Unless specified otherwise, borderline and abnormal ECG findings that require additional local workup do not require waiver if the additional workup is reviewed by the ECG Library as acceptable (normal/normal variant). If ACS evaluation or AFMOA/MAJCOM waiver is required for any of the findings, the ECG library will indicate this in its correspondence. **Unless indicated clinically, only the tests requested by the ECG library need to be performed.** 

In general, these recommendations are intended to guide the aeromedical evaluation of the asymptomatic aviator with an electrocardiographic finding. The aviator who presents with symptoms, signs or findings of potential clinical significance must first be managed locally as a clinical patient. These ECG guidelines are based on historic ACS data as well as the 2017 International criteria for ECG interpretation in athletes. \*denotes new aircrew disposition guidelines based on published and ACS data since the last ECG disposition guide.

Electronic submission of cardiac studies to the ECG library is preferred with average disposition time in less than 24 hours. Upload studies at <a href="https://acspacs.area52.afnoapps.usaf.mil/PicomCloud/Default">https://acspacs.area52.afnoapps.usaf.mil/PicomCloud/Default</a>. You may contact the ECG library to gain access or for any questions at USAFSAM.FECIECGLib@us.af.mil.

## **Normal or Normal Variant ECG Findings**

The following are considered normal or normal variants in our aviator population. **No further evaluation** or follow up is needed for these findings **IF ISOLATED** (two or more normal variant or borderline findings requires additional testing after ACS ECG library disposition).\*

| bpm   | 002.             | Sinus bradycardia (30 to 50 beats per minute) Note: Aeromedically, normal sinus rhythm is defined as 50-100          |
|-------|------------------|--|
|       | 007.             | Sinus arrhythmia   |
|       | 028.             | Ectopic atrial rhythm  |
|       | 040.             | Accelerated junctional rhythm  |
|       | 080.             | Supraventricular rhythm at a rate of less than 100 bpm   |
|       | 085.             | Wandering atrial pacer   |
|       | 104.             | Second degree AV block, Mobitz Type I (Wenckebach)   |
|       | 121.             | Incomplete right bundle branch block   |
|       | 123.             | Terminal conduction delay (S wave in the lateral leads $\geq$ 40 msec)   |
|       | 132.             | Nonspecific intraventricular conduction delay, QRS $\geq$ 100 but $<$ 120 msec                                       |
|       | 204.             | ST segment elevation due to early repolarization   |
| norma | 221.<br>al ECG 1 | Persistent juvenile T-waves (T wave inversions in V1-3 in an otherwise that have been present on all previous ECG's) |
|       | 737.             | Indeterminate QRS axis   |
|       | 743.             | S1, S2, S3 pattern (S waves in the inferior limb leads)  |
|       | 744.             | S1, S2, S3 pattern with RSR' pattern in V1 or V2 with QRS < 120 msec   |
|       | 755.             | R > S in V1 without other evidence of right ventricular hypertrophy  |
|       | 764.             | RSR' pattern in V1 or V2 with QRS < 120 msec   |
| 10.5m | 721.<br>nV1)     | Right ventricular hypertrophy (R wave in V1 plus S wave in V5 or V6 >  |

# **Abnormal or Possibly Abnormal ECG Findings**

The following are abnormal or possibly abnormal ECG findings with brief explainations and disposition. Each disposition if based on the associated finding **in isolation** (two or more abnormal findings requires ACS ECG library review).

Marked Sinus Bradycardia: Sinus bradycardia refers to heart rate less than 60 bpm with marked sinus bradycardia heart rate less than 30bpm. Marked sinus bradycardia is usually the result of athletic conditioning with increased vagal tone and is not associated with an adverse prognosis. Past evaluation of this finding in asymptomatic aviators by the ECG Library has consistently failed to uncover evidence of sinus node dysfunction unless heart rate is less than 30bpm. Further evaluation should be pursued as clinically indicated and/or requested by the ECG Library and commonly includes verification of increased heart rate with exercise.

A02. Marked sinus bradycardia (<30 bpm)\*

**Sinus Tachycardia:** Sinus tachycardia may be transient and due to anxiety, fever, pain, etc. It may occasionally be an indicator of underlying heart disease or a metabolic abnormality. If sinus tachycardia is noted on an ECG, a repeat ECG should be obtained. If this is a persistent finding on the repeat ECG, a Holter monitor should be obtained while the aviator remains on flying status (no DNIF). If sinus tachycardia persists on the Holter, further evaluation should be pursued as clinically indicated and/or requested by the ECG Library.

001. Sinus tachycardia (resting heart rate > 100 bpm)

#### **Short PR Interval:**

Short PR interval (PR < 120 msec) may be a normal variant but is occasionally evidence for a bypass tract, even without an accompanying delta wave. Before diagnosing short PR interval, one must assure that it is truly sinus rhythm with sinus origin P waves, rather than ectopic atrial or other rhythm. For a PR interval between 100 and 120 msec, it is most likely a normal variant, but could represent a bypass tract. For these cases, a thorough history should be obtained locally with specific questions aimed at the detection of tachyarrhythmias, to include palpitations, rapid heart beat sensations, lightheadedness or syncope. If the history is unremarkable with no suggestion of a possible tachyarrhythmia, then no further evaluation is indicated and the finding should be considered a normal variant. For a PR interval less than 100 msec, the possibility of a bypass tract is much greater and further evaluation should be pursued as clinically indicated and/or requested by the ECG Library

029. Short PR interval (PR interval < 120 msec in all leads)

#### **Wolff-Parkinson-White:**

Ventricular Pre-excitation to include Wolff-Parkinson-Whitepattern on ECG requires ACS evaluation/review. The aviator/aircrew should be placed DNIF pending ACS evaluation/review. See the *Wolff-Parkinson-White (WPW) and Other Pre-excitation Syndromes* Waiver Guide for further details.

- 704. Wolff-Parkinson-White pattern
- 705. Lown-Ganong-Levine pattern

## **Prolonged QT Interval:\***

Perform a repeat fasting ECG on a separate day and submit both ECGs to the ECG Library with a list of any prescription or over-the-counter medications and supplements used. Electrolytes to include potassium, magnesium, and calcium should also be checked. Further guidance will follow ECG Library review of this information. Per new ECG guidelines in athletes, corrected prolonged QTc duration has increased from prior guidelines.

215. Prolonged QT defined as a QTc >470 msec in males or >480 msec in females.

## Atrial Enlargement/Abnormality:\*

The following are nonspecific as isolated ECG findings in isolation. Additional testing (echocardiogram +/- stress test) is necessary only when accompanied by axis deviation, fasicular block, or bundle branch block. Further testing necessary is based on clinical indications by the interpreting physician at the ECG Library.

- 500. Left atrial enlargement
- 501. Right atrial enlargement
- 503. Biatrial enlargement

**Ventricular Hypertrophy:** An echocardiogram is required for evaluation of all ventricular hypertrophy with the exception of isolated right ventricular hypertrophy. If the echocardiogram is normal or normal variant by ECG Library review, no further workup is necessary. Since the specificity of these findings on ECG is poor, the aviator does not need to be DNIF pending our interpretation of the echocardiogram. For any left ventricular hypertrophy also provide a detailed exercise and blood pressure history for the past 6-12 months.

- 720. Left ventricular hypertrophy by voltage criteria with associated ST segment abnormalities
  - 727. Biventricular hypertrophy

729. Left ventricular hypertrophy by voltage alone (sum of the S wave voltage in V1 or V2 plus the R wave voltage in V5 or V6 > 55 millivolts for individuals 35 years old or younger or > 45 millivolts for individuals older than 35 years of age).

## First Degree AV Block:

First degree AV block is most often the result of athletic conditioning with increased vagal tone. This finding is common and not associated with an adverse prognosis. Past evaluation of this finding by the ECG Library has consistently failed to uncover evidence of conduction system disease. Therefore, evaluation of this finding is only required if requested by the interpreting physician or for very prolonged PR interval (>400ms).\*

100. First degree AV block. (PR interval  $\geq$  220 msec.)

## Second Degree Mobitz Type II, and Third Degree AV Block:

The following abnormalities, if confirmed by the ECG Library or local consultant, are disqualifying for flying duties and waiver is not recommended. ACS evaluation is not required. Local medical evaluation and management is mandatory. Mobitz Type I second degree AV block (Wenckebach block) is considered a normal variant and is listed as such above.

- 105. Second degree AV block, Mobitz Type II
- 108. Complete heart block. This must be differentiated from A-V dissociation due to sinus bradycardia with a competing junctional rhythm, which may be a normal variant finding.

## **Right Bundle Branch Block:**

This recommendation includes new complete right bundle branch block or complete right bundle branch block that has progressed from previous incomplete right bundle branch block. An echocardiogram is required for evaluation. If a previous echocardiogram is on file at the ACS, it may be acceptable per judgment of the ECG Library physician. The aviator does not need to be DNIF during this evaluation. Reminder - incomplete right bundle branch block in isolation is a normal variant and does not require evaluation.

120. Right bundle branch block with normal QRS axis.

#### **Left Bundle Branch Block:**

Left bundle branch block requires ACS evaluation and waiver. The aviator/aircrew should be placed DNIF pending ACS evaluation. The primary physician should insure that the aviator is clinically stable prior to arranging an ACS evaluation. See the *Left Bundle Branch Block* Waiver Guide for further details.

124. Left bundle branch block

## Fascicular blocks and Axis Deviation:

Isolated Axis deviation is a normal variant unless accompanied by any other abnormal, borderline, or even normal variant ECG finding (such as complete or incomplete RBBB, atrial enlargement, or ventricular enlargement) then further evaluation should be pursued as requested by the ECG Library.\* Fascicular blocks require echocardiogram at all ages and if age >35 then exercise stress. Waiver is no longer required unless the echo or stress test are abnormal after ACS/ECG library review.

The diagnostic criteria and evaluation of hemiblocks and left axis deviation are as follows:

126. Left anterior fasicular block (LAFB):

Displacement of the mean QRS axis in the frontal plane to between  $-45^{\circ}$  and  $-90^{\circ}$ , and

A qR complex in leads I and AVL, an rS complex in leads II, III

and AVF, and

and AVF, and

normal or only slightly prolonged QRS duration.

128. Left posterior fasicular block (LPFB):

Displacement of the mean QRS axis in the frontal plane to between  $+120^{\circ}$  and  $+180^{\circ},$  and

An rS complex in leads I and AVL, a qR complex in leads II, III

normal or only slightly prolonged QRS duration

735. Left axis deviation (LAD):

QRS axis -30° or more negative without full criteria for LAH as

736. Right axis deviation (RAD)

QRS axis +120° or more positive without criteria for left posterior

hemiblock

above.

**Supraventricular and Ventricular Ectopy and Pairing:** Holter monitor is required for one or more paired premature beats and for two or more isolated premature beats on a single page of ECG paper, 12- lead or rhythm strip, regardless of the age of the aviator/aircrew.\* Further evaluation should be pursued as clinically indicated and/or requested by the ECG Library after holter monitor review.

- 023. Premature atrial beat (PAC), two or more on a single page of ECG paper, 12- lead or rhythm strip
- 043. Premature junctional beat (PJC), two or more on a single page of ECG paper, 12- lead or rhythm strip
- 083. Premature supraventricular beat, two or more on a single page of ECG paper, 12- lead/rhythm strip

- 063. Premature ventricular beat (PVC), two or more on a single page of ECG paper, 12- lead/rhythm strip
- 032. Paired atrial premature beats, one or more pairs on a single page of ECG paper
- 046. Paired junctional premature beats, one or more pairs on a single page of ECG paper
- 072. Paired ventricular premature beats, one or more pairs on a single page of ECG paper

## **Supraventricular Tachycardias & Arrhythmias:**

Any individual with documented supraventricular tachycardia (three or more supraventricular premature beats in a row at a rate exceeding 100 bpm) or multifocal tachycardia requires holter monitor. Member need not routinely be placed DNIF if there are no associated hemodynamic symptoms. Atrial fibrillation and atrial flutter require cardiology evaluation and DNIF.

- 021. Atrial tachycardia
- 026. Atrial fibrillation
- 027. Atrial flutter
- 036. Multifocal atrial tachycardia (MAT)
- 041. Junctional tachycardia (> 100 bpm)
- 081. Supraventricular tachycardia

**Ventricular Tachycardia:** An aviator/aircrew with asymptomatic nonsustained ventricular tachycardia should be placed DNIF. One 24 hour Holter monitor should be obtained. ACS review/evaluation is required for waiver consideration of any ventricular tachycardia.

061. Ventricular tachycardia (three or more ventricular beats in a row at a rate > 100 bpm)

**Ventricular Fibrillation and Ventricular Flutter:** The following abnormalities are disqualifying for continued flying duties. Waiver is not recommended, and ACS evaluation is not required.

066. Ventricular fibrillation

#### 067. Ventricular flutter

## **Findings Suggestive of Myocardial Infarction:**

ECG findings diagnostic for or very suggestive of myocardial infarction are disqualifying for continued flying duties pending further evaluation. The individual should have a cardiology evaluation to insure that he is clinically stable. If a true myocardial infarction is confirmed, this is disqualifying for flying duties but may be waiver eligible after ACS evaluation (see waiver guide).

All 600 series codes. Myocardial infarction

The aviator may remain on flying status during evaluation of the following more nonspecific findings:

- 739. Non-diagnostic Q waves. No further evaluation is required unless directed by the ECG Library.
- 759. Poor R wave progression. This finding may be due to incorrect chest lead placement or can be a normal variant. It can also be seen in myocardial infarction. Evaluation consists of repeat ECG with attention to chest lead placement and other testing as directed by the ECG Library. Echocardiogram may be requested to rule out wall motion abnormalities.

## 18. ST Segment and T Wave Abnormalities:

The following diagnoses may be normal variants, or may be findings associated with myocardial ischemia, cardiomyopathy and other disorders. The nonfasting state may cause nonspecific ST-T wave changes on ECG. If these findings represent a serial change and persist after repeat <u>fasting</u> ECG, a treadmill exercise tolerance test and echocardiogram should be performed on aviators aged 35 or older. For aviators younger than 35 years, an echocardiogram should be performed. If a previous screening echocardiogram is on file at the ACS, it may be acceptable per judgment of the ECG Library physician. Since mild ST segment and T wave abnormalities are not very specific, the aviator does not need to be DNIF during this evaluation. However, judgment should be exercised in aviators with more than mild changes or compelling coronary risks.

- 200. Low T waves less than 2 mm in chest leads V3-V6 or less than 0.5 mm in limb leads I and II.
  - 201. Nonspecific T wave abnormalities
  - 203. Nonspecific ST segment depression

## 19. Cardiac Inflammation (Pericarditis and Myocarditis):

If pericarditis or myocarditis is clinically present, the aviator should be placed DNIF and should be treated as indicated by the clinical condition. Confirmation should be done locally and studies sent to ACS ECG library for review. If asymptomatic, ECG

confirmation can be done throught ECG library and further evaluation pursued as clinically indicated and/or requested by the ECG Library

- 706. Compatible with pericarditis
- 707. Compatible with myocarditis

# **Miscellaneous**

## **Treadmill Test Results:**

In order to insure a consistent interpretation of all studies and to attain the highest sensitivity, the following criteria were established for classifying treadmill exercise tolerance test results. The ST segment depression will be read at 80 msec after the J point irrespective of ST segment slope. The PQ segment will be used as the baseline. Tests showing less than 0.5 mm of ST segment depression are considered normal. Tests showing 0.5 to 0.9 mm of ST segment depression are considered borderline. Tests showing 1 mm or more of ST segment depression are abnormal. Any studies considered to be abnormal by review at the ECG Library will require an ACS evaluation.

Treadmill testing may also be suggestive of organic heart disease due to findings other than ST segment depression. These may include exercise-induced chest discomfort, hypotensive blood pressure response to exercise, chronotropic incompetence with decreasing heart rate at peak exercise or exercise-induced dysrhythmias. Exercise-induced dysrhythmias should be treated as described in the appropriate sections of this document and corresponding waiver guide.

The treadmill test should be performed in the fasting state. Baseline ECGs should be obtained supine, standing, and after hyperventilation. If ST segment depression is present on any baseline ECG, 1 mm of additional ST segment depression beyond the baseline ST segment will be required to be considered abnormal. The **raw unprocessed tracings and interpreted report** must be forwarded to the ECG Library for review.

# **Holter Monitor Findings:**

A Holter monitor is generally performed to evaluate rhythm or conduction disturbances found on physical exam or 12-lead ECG or subjective complaints of palpitations. It might be requested by the ECG Library or ordered by a local provider. The following discussion assumes no associated hemodynamic symptoms and addresses the aeromedical disposition of isolated ectopy and ectopic pairs. Disposition of other findings, such as supraventricular tachycardia, are discussed in appropriate sections of this document.

By ECG Library review, if isolated ectopic beats on the Holter are frequent or less ( $\leq$  10% of total beats) and if ectopic pairs are occasional or less (10 total pairs or fewer), no further testing is required and the findings are aeromedically acceptable without waiver.

If ectopic beats are very frequent (>10% of total beats) and/or ectopic pairs are frequent (>10 pairs total), a treadmill test and echocardiogram should be performed with

appropriate reports and tracings/images referred to the ECG Library for review. The aviatior does not need to be DNIF during this assessment.

# **Echocardiograms:\***

Actual echocardiogram images must be sent to the ACS for review. Reports without images are not accepted. Echocardiograms must include at minimum M-mode, 2-dimensional and Doppler studies. Studies should be saved in a digital format and preferably uploaded into the ECG library system as above. VHS studies are no longer accepted. CD/DVD studies can be mailed only if unable to upload into ECG library and this can delay processing time by as much as two weeks.

Published by the US Air Force Aeromedical Consultation Service Central Electrocardiographic Library Last updated: Nov 2017 (Note: This reference is published as a guide only, final ECG disposition recommendations are determined by the ECG Library as per AFI 48-123.)

### WAIVER GUIDE

Updated: Sep 2015

Supersedes Waiver Guide of Mar 2011

By: Dr Dan Van Syoc

Reviewed by Lt Col Eddie Davenport, Chief ACS Cardiologist

## **CONDITION:**

Ectopy, Supraventricular and Ventricular, and Pairing (Sep 2015)

## I. Waiver Consideration.

Symptomatic ectopy which is significant enough to interfere with satisfactory performance of duty or requiring any medication for control is disqualifying for all flying classes as well as retention. For asymptomatic ectopy, waiver is not required if further evaluation specified by and reviewed by the ECG Library discloses no other disqualifying conditions.

Table 1: Policy for asymptomatic supraventricular and ventricular ectopy and

pairing

| Findings on<br>24-hour<br>Holter       | Additional Local<br>Testing        | Flying Class/<br>Waiver Required<br>Waiver Authority# | ECG Library<br>makes final<br>determination | ACS<br>Review/<br>Evaluation |
|--|------------------------------------|---|---|------------------------------|
| PACs/PVCs<br>≤10% and/or<br>1-10 pairs | None                               | FC I/IA<br>No<br>AETC                                 | Yes   | No                           |
|  |                                    | FCII/III and<br>ATC/GBO/SWA<br>No<br>MAJCOM           | Yes   | No                           |
| PACs/PVCs<br>>10% and/or<br>>10 pairs  | Echocardiogram and treadmill test* | FC I/IA, II/III<br>No (if normal studies)<br>AETC     | Yes   | Yes                          |
|  |                                    | ATC/GBO/SWA<br>No (if normal studies)<br>MAJCOM       | Yes   | No                           |

<sup>\*</sup> Studies to be submitted to the ECG library, if found aeromedically acceptable no further work-up required.

AIMWTS search in Sep 2015 revealed 155 cases carrying a diagnosis of supraventricular and ventricular ectopy and pairing. There were 22 cases that were disqualified. Breakdown of the cases revealed: 4 FC I/IA cases (3 disqualified), 102 FC II cases (13 disqualified), 42 FC III cases (4 disqualified), 6 ATC/GBC cases (2 disqualified), and 1 MOD cases. Most of the disqualifications were due to other cardiac diagnoses.

## II. Information Required for Waiver Submission.

None, unless other disqualifying findings are found on further evaluation performed clinically or as specified by the ECG Library. In those cases, refer to the applicable waiver guide and/or as directed by the ECG Library. For symptomatic ectopy/pairing that is significant enough to interfere with satisfactory performance of duty, ensure MEB results are included in AMS.

## III. Overview.

This waiver guide discusses isolated ectopy and paired ectopy (pairs, couplets) and assumes no associated hemodynamic symptoms. Supraventricular and ventricular tachyarrhythmias are discussed in separate waiver guides. Ectopy and pairs include premature supraventricular and premature ventricular contractions (PVCs). In this discussion, the term ectopy will refer to both supraventricular and ventricular ectopy unless otherwise specified. Supraventricular ectopy includes premature atrial contractions (PACs) and premature junctional contractions (PJCs). The term PAC will be used to refer to all supraventricular ectopy.

Ectopy is quantified as a percentage of total beats on a Holter monitor and is graded as rare (<0.5%), occasional (0.5% - 1%), frequent (>1%), and very frequent (>10%). Pairs are similarly graded as rare, occasional, or frequent by total number of pairs on a Holter monitor. Aeromedical disposition is determined by the grading of ectopy and pairs on a Holter monitor. Typically, Holter monitor will have been requested to evaluate ectopy on a 12-lead electrocardiogram, ectopy appreciated during physical examination, or to evaluate subjective complaints of palpitations.

On 12-lead electrocardiogram (ECG), PACs have been reported in about 0.6% of aviators and 0.4%-3.0% of civilian populations. PVCs have been reported in about 0.8% of aviators and 2.0%-7.0% of various civilian populations. Evaluating ectopy on 12-lead ECG is thus not a problem of large numbers but is nevertheless made difficult by the significant frequency of ectopy reported on 24-hour Holter monitors performed on apparently healthy subjects. Holter findings were reported on 303 male military aviators with no structural heart disease and no referral diagnoses of arrhythmia; only 12% had no ectopy. Rare and occasional PACs and PVCs occurred in about 75% and 50%, respectively. Frequent PACs and PVCs only occurred in about 2.5% and 3.5%, respectively. PAC pairs occurred in about 15%. Otherwise, more complex ectopy was unusual.

The presence of more than one PAC and/or PVC in 10 seconds (standard 12-lead ECG page) requires additional evaluation with a 24-hour Holter as outlined in the following table. DNIF is not required pending the 24-hour Holter.

Table 2: Guide to necessity for Holter monitor

| ECG/Rhythm Strip       | 24-hour Holter Required <sup>1</sup> |
|------------------------|--------------------------------------|
| PACs, PJCs < 2         | No                                   |
|                        |                                      |
| PACs, PJCs ≥2          | Yes                                  |
| Paired PAC, PJC or PVC | Yes                                  |
| $\geq 1$               |                                      |

<sup>&</sup>lt;sup>1</sup> Holter monitor results to include **interpreted report summary**, **representative tracings**, **and patient diary** must be forwarded to ECG library.

In summary, Holter monitor is required for two or more isolated premature beats and for one or more paired premature beats on a standard (10-second) single page of ECG paper, 12- lead or rhythm strip, regardless of the age of the aviator/aircrew. Holter monitor is no longer required for one isolated atrial, junctional or ventricular premature beat on a single page of ECG paper, 12- lead or rhythm strip.

The results of the 24-hour Holter will determine requirement for further work-up. IAW AF policy, waiver for isolated and paired ectopy is not required for any class of flying duties if local evaluation specified by and reviewed by the ECG Library discloses no other disqualifying findings. By ECG Library review, if isolated ectopic beats on the Holter are frequent or less (< 10% of total beats) and if ectopic pairs are occasional or less (10 total pairs or fewer), no further testing is required and the findings are aeromedically acceptable and considered normal variant. If ectopic beats are very frequent (>10% of total beats) and/or ectopic pairs are frequent (>10 pairs total), a treadmill test and echocardiogram should be performed with appropriate reports and tracings/images referred to the ECG Library for review. The aviator does not need to be DNIF during this assessment.

#### IV. Aeromedical Concerns.

If isolated or paired ectopy itself causes hemodynamic symptoms, then aeromedical disposition is determined by the symptoms as well as by the presence and severity of underlying heart disease. In the absence of hemodynamic symptoms, there are three basic aeromedical concerns. One, does the ectopy represent a risk for sustained tachydysrhythmias? Two, does the ectopy represent a risk for cardiac events? And three, does the ectopy predict underlying cardiac disease?

In an ACS database of 430 aviators evaluated for nonsustained or sustained supraventricular tachycardia (SVT), frequent PACs, PAC pairs and nonsustained SVT were not predictive of hemodynamically symptomatic SVT or of recurrent sustained SVT. In a similar database of 193 aviators with nonsustained ventricular tachycardia, neither frequent PVCs nor PVC pairs predicted sustained ventricular tachycardia or associated hemodynamic events. These data suggest that frequent isolated ectopy and paired ectopy do not present an increased risk for tachyarrhythmic events in the absence of structural heart disease.

The predictive value of ectopy for underlying cardiac disease is less clear. The considerable frequency and variability of ectopy in normal subjects makes it difficult to

determine its predictive value for disease. PACs may occur in association with some disease states, such as mitral valve prolapse, but prognosis is not related to the PACs. On the other hand, frequent and complex PVCs in the presence of coronary and some other heart diseases clearly confer a poorer prognosis. This is true in clinical populations with significant, usually symptomatic disease. It may be less so in asymptomatic populations such as aircrew. However, some ACS databases do suggest increased prevalence of cardiac disease in the presence of significant ectopy.

| ICD-9 ( | ICD-9 Codes for Supraventricular and Ventricular Ectopy And Pairing |  |
|---------|---|--|
| 427.60  | Premature beats unspecified   |  |
| 427.61  | Supraventricular premature beats                                    |  |
| 427.69  | Other premature beats   |  |

| ICD-10 | ICD-10 Codes for Supraventricular and Ventricular Ectopy And Pairing |  |
|--------|--|--|
| I49.4  | Unspecified premature depolarization                                 |  |
| I49.1  | Atrial premature depolarization                                      |  |
| I49.2  | Junctional premature depolarization                                  |  |
| I49.49 | Other premature depolarization                                       |  |

#### V. References.

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# Eczematous Dermatitis (Eczema) and Atopic Dermatitis (Dec 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

**Significant Changes:** Updated to reflect MSD changes. Waiver tolerance for untrained applicants expanded.

## I. Waiver Consideration

Eczematous (Eczema), atopic dermatitis, or any other skin condition that is severe enough to require frequent absence from duty, interfere with the wearing of operational equipment, or uncontrolled despite adequate treatment with career field approved medications are disqualifying for all flying classes, ground-based operators, and special duty operators including for retention. Controlled eczema or atopic dermatitis with career field approved medications is not disqualifying for ATC or GBO duties. Eczema or atopic dermatitis requiring chronic topical corticosteroid therapy for symptomatic control is disqualifying for FC I/IA/II/III and special warfare duties. A history of eczema or atopic dermatitis after the twelfth birthday is also disqualifying for FC I/IA. Factors considered when accessing suitability for waiver include the severity of disease, evidence of active lesions, the risk associated with specific medication(s), the individual service member's tolerance of the medication(s) and adherence to therapy, and the presence of comorbid conditions (i.e., asthma, allergic rhinitis, and food allergies).

A policy memo released by SECAF in Jan 2017 allowed for select candidates medically classified as having mild forms of eczema to be processed for an accession waiver. Therefore, select FC I/IA and untrained applicants in all flying classes with active disease are eligible for waiver on a case-by-case basis if the disease is mild. Moderate to severe disease exceeds current waiver threshold for untrained personnel. Mild disease is defined aeromedically as disease that is controlled with the use of emollients or occasional low-tomoderate potency steroids, disease with no other significant disqualifying comorbidities, and/or disease that does not require more than annual dermatology visits. Moderate to severe disease is defined aeromedically as disease that is controlled with the use of chronic topical steroids or intermittent high potency steroids, disease controlled with use of systemic medications or phototherapy, disease that interferes with sleep or wearing of military equipment, disease with significant disqualifying comorbidities, and/or disease requiring more than annual dermatology evaluation. Additionally, FC I/IA applicants require pre- and post-bronchodilator spirometry testing prior to waiver submission to exclude the presence of comorbid pulmonary dysfunction. Abnormal pulmonary screening results should prompt full pulmonary function testing and further evaluation.

Members eligible for waiver will be considered once the individual demonstrates tolerability of the current treatment regimen, reduction of any distracting symptoms, and the ability to wear operational equipment. Initiation of treatment that is not on the approved career field medication list is disqualifying for all flying classes, ground base operators, and special duty operators. Systemic therapy with oral glucocorticoids, oral immunomodulators, or PUVA phototherapy for disease control exceeds historic waiver

thresholds. UVB phototherapy is less toxic than PUVA phototherapy and can be considered on a case-by-case basis.

**Table 1: Waiver potential for Eczema/Atopic dermatitis** 

|              | Potential for Eczema/Atopic dern  | ·                          | A CC D        |
|--------------|---|----------------------------|---------------|
| Flying Class | Condition   | Waiver Potential<br>Waiver | ACS Review or |
| (FC)         |   | Authority                  | Evaluation    |
| I/IA         | Active eczema or atopic dermatitis, mild <sup>1,2</sup>   | Yes<br>AETC                | Yes           |
|              | Active eczema or atopic dermatitis, moderate to severe <sup>1,3</sup>   | No<br>AETC                 | No            |
|              | Verified history of eczema or atopic dermatitis after twelfth birthday <sup>1</sup>   | Yes<br>AETC                | Yes           |
| II/III/SWA   | Eczema, atopic dermatitis, or other skin condition when severe enough to require frequent absence from duty, interfere with the wearing of operational equipment, or uncontrolled despite adequate treatment with aeromedically approved medications <sup>4,5</sup> | No<br>MAJCOM               | No            |
|              | Eczema or Atopic dermatitis treated with topical steroids (chronic usage), topical pimecrolimus, or topical tacrolimus  | Yes<br>MAJCOM              | No            |
|              | Eczema or atopic dermatitis treated with emollients or occasional topical steroids is not disqualifying   | N/A                        | N/A           |
| GBO/ATC      | Eczema, atopic dermatitis, or other skin disorder when severe enough to require frequent absence from duty, interfere with the wearing of operational equipment, or uncontrolled despite adequate treatment with career field approved medications <sup>4,5</sup>   | No<br>MAJCOM               | No            |
|              | Eczema or Atopic dermatitis treated with topical pimecrolimus or topical tacrolimus   | Yes<br>MAJCOM<br>N/A       | No N/A        |

| Eczema or atopic dermatitis treated    |  |
|--|--|
| with emollients or topical steroids is |  |
| not disqualifying                      |  |
|  |  |
|  |  |
|  |  |

- 1 FC I/IA applicants require pre- and post-bronchodilator spirometry testing prior to waiver submission.
- 2 Mild disease is defined aeromedically as disease that is controlled with the use of emollients or occasional low/medium potency steroids, disease with no other significant disqualifying comorbidities, and/or disease that does not require more than annual dermatology visits.
- Moderate to severe disease is defined aeromedically as disease that is controlled with the use of chronic topical steroids or intermittent high potency steroids, disease controlled with use of systemic medications or phototherapy, disease that interferes with sleep or wearing of military equipment, disease with significant disqualifying comorbidities, and/or disease requiring more than annual dermatology evaluation.
- 4 Eczema or atopic dermatitis requiring treatment with any medication not included on the applicable career field approved medication list is disqualifying, and the waiver authority is AFMRA if waiver is being entertained.
- 5 Systemic therapy with oral glucocorticoids, oral immunomodulators, or PUVA phototherapy for disease control exceeds historic waiver thresholds. UVB phototherapy may be considered for waiver.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

# A. Initial Waiver Request:

- 1 Summary of presentation, course, and treatment.
- 2 Consultation reports form all treating providers or specialists, which should include:
  - a. Subjective symptoms and objective physical exam findings to include thorough skin exam.
  - b. Tolerability and doses of current treatment regimen.
    - i. For topical steroids use include the formulation, potency, total dose, treatment duration, site of application, and any evidence of skin thinning (telangiectasia, etc.)
  - c. Documentation excluding other atopic syndromes (i.e, asthma, allergic rhinitis, food allergies)
  - d. FC I/IA applicants required to have pre- and post-bronchodilator spirometry testing.
- 3 Any specific diagnostic tests performed, before and after treatment.
- 4 Current physical examination findings.
- 5 FL4 with RTD and ALC status, if applicable.
- 6 Any other pertinent information.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - b. Current symptoms and development of any disease flares.
  - c. Current medications, doses, and adverse effects.
    - i. For topical steroids use include the formulation, potency, total dose, treatment duration, site of application, and any evidence of skin thinning (telangiectasia, etc.)
  - d. Current physical examination findings to include thorough skin exam.
- 2 Any interval diagnostic tests performed.
- 3 Any other pertinent information.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Eczematous (Eczema) or atopic dermatitis (AD) are relatively common conditions defined by chronic inflammation of the skin. It is primarily seen in prepubescence, but it can persist into or develop in adolescence or adulthood. Presentation can vary from very mild disease requiring no treatment or only topical emollients to severe disease requiring systemic immunotherapy therapy for symptomatic control. Common symptoms include dry and pruritic skin rashes affecting the skin flexures, hands, neck, or face (although any area of the body can be involved). If uncontrolled, discomfort from pruritus or pain can be significant and the resulting distraction may jeopardize flight safety or operational duties. Active disease might interfere with wear of operational or flight equipment. Additionally, the environmental condition and stressors attendant to aviation and operational duties or deployment to austere environments potentially results in disease flares.

Eczema and AD are associated with several aeromedically significant comorbidities including asthma, allergic rhinitis, and food allergies. A thorough evaluation should be documented to assess for these associated atopic diseases. A 2017 retrospective study involving 3966 children found those who developed AD in adolescence had a 30% cumulative incidence of developing asthma. Thus, FC I/IA applicants who have a history of eczema or atopic dermatitis after the twelfth birthday or current active eczema or atopic dermatitis should have full pre- and post-bronchodilator spirometry test done prior to waiver submission. Abnormal results should prompt appropriate clinical evaluation.

The use of systemic immunotherapy such as oral glucocorticoids, cyclosporine, or PUVA have traditionally not been recommended for waiver given the unacceptable adverse effects and underlying disease severity. Psoralen plus ultraviolet A (PUVA) photochemotherapy carries significant short-term and long-term side effects. Short-term side effects include nausea, dizziness, headache, and photosensitivity. Long term side effects include pruritus, skin damage, and increased skin cancer risk. Broad-spectrum ultraviolet B (UVB) phototherapy is better tolerated without the adverse effect profile of PUVA. This therapy is deemed acceptable and its use has waiver potential. UVB therapy may require several treatments per week and potentially results in mobility restrictions if the treatment is necessary to maintain disease control. Topical corticosteroids are

frequently used and are typically well tolerated. Prolonged use of topical steroids increases the risk of systemic adverse effects such as suppression of the hypothalamic-pituitary-adrenal axis, iatrogenic Cushing's syndrome, avascular necrosis, and glaucoma. Low or moderate potency steroids and intermittent use mitigates these risks.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 110 individuals with an AMS containing the diagnosis of Eczematous Dermatitis. Twelve individuals (7.3%) were disqualified. A breakdown of the cases was follows: 27 FC I/IA cases (8 disqualified), 40 FC II cases (0 disqualified), 37 FC III cases (4 disqualified), 2 ATC/GBC cases (0 disqualified), 0 MOD cases, and 4 RPA Pilot cases (0 disqualified).

| ICD-9 codes for Eczema/Atopic Dermatitis |  |
|--|--|
| 691.8                                    | Atopic dermatitis and related conditions |
| 692.9                                    | Contact dermatitis and other eczemas     |

| ICD-10 codes for Eczema/Atopic Dermatitis |  |
|---|--|
| L20.9                                     | Atopic dermatitis, unspecified (includes eczema) |
| L30.9                                     | Dermatitis, unspecified                          |

# **IV. Suggested Readings**

- 1. Lee JH, Son SW, and Cho SH. A Comprehensive Review of the Treatment of Atopic Eczema. Allergy Asthma Immunol Res, 2016; 8(3): 181-190.
- 2. Wong IT, Tsuyuki RT, et al. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. Can Pharmacists J, 2017; 150(5): 285-297.
- 3. Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, et al. Guidelines of care for the management of atopic dermatitis. J Am Acad Derm, 2015; 71(6). https://www.aad.org/practicecenter/quality/clinical-guidelines/atopic-dermatitis
- 4. Wan J, Mitra N, et al. Variations in risk of asthma and seasonal allergies between early and late onset pediatric atopic dermatitis: a cohort study. J Am Acad Derm, 2017; 77(4):643-640.
- 5. World Health Organization Classification of Topical Corticosteroids. https://emedicine.medscape.com/article/2172256-overview

## **Endometriosis (Feb 2019)**

Reviewed by Maj Hattie McAviney (RAM 20), Dr. Dan Van Syoc (Deputy Chief, ACS), Lt Col Jason Massengill (AF/SG consultant for OB/GYN), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New format.

#### I. Waiver Consideration

Any history of endometriosis is disqualifying for FC I/IA and SWA duties. Endometriosis is disqualifying for retention, as well as for all flying and special duty classes when it results in an inability to perform duties, causes frequent absences from duty, or requires the need for ongoing specialty f/u more than annually.

**Table 1: Waiver potential for endometriosis** 

| Flying Class | Medication/Treatment                   | Waiver        | ACS               |
|--------------|--|---------------|-------------------|
|              | Required                               | Potential     | Review/Evaluation |
|              | for Symptom Control of                 | Waiver        |                   |
|              | Endometriosis                          | Authority     |                   |
| I/IA         | Any documented history of              | No            | No                |
|              | endometriosis regardless of            | AETC          |                   |
|              | treatment <sup>1</sup>                 |               |                   |
| II/III       | NSAIDs, estrogen/progesterone          | Yes           | No                |
| ATC/GBO/SWA  | combinations, DepoProvera <sup>2</sup> | MAJCOM        |                   |
|              | Danazol, GnRH <sup>3</sup>             | No<br>AFMRA   | No                |
|              | Surgery                                | Yes<br>MAJCOM | No                |

<sup>1.</sup> Also applicable to SWA personnel with waivers considered on a case-by-case basis similar to trained FC II & FC III personnel.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

<sup>2.</sup> All medications and medication combinations need to be themselves approved for use in aircrew.

<sup>3.</sup> GnRH-gonadotropin releasing hormone agonists.

## A. Initial Waiver Request:

- 1 Summary of presentation, course, and treatment, to include a complete history of symptoms and degree to which they incapacitate the patient.
- 2 Reports of any pertinent laboratory studies, including the most recent hematocrit.
- 3 Gynecology consultation report, including follow-up notes with examination findings after treatment/resolution.
- 4 Any specific diagnostic tests performed, before and after treatment (as indicated).
- 5 Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 6 Current physical examination findings.
- 7 FL4 with RTD and ALC status, if member did not meet retention status.
- 8. Any other pertinent information.
- 9. The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

# B. Renewal Waiver Request:

- 1 Interval history including treatments, tolerance, and any adverse side effects.
- 2 All applicable labs, particularly most recent hematocrit.
- 3 Consultation report from gynecologist or primary care physician.
- 4 The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

#### III. Aeromedical Concerns

Endometriosis is a progressive disease and there is little correlation between the physical extent of the disease and severity of symptoms women report. The pain associated with endometriosis usually begins as low grade discomfort and may progress over hours or days to a severe discomfort or pain that may be distracting. The pain may initially be predictable and occur in a cyclic perimenstrual fashion, but often progresses over time. Symptoms of endometriosis often require control with aeromedically approved medications. In these cases, it is not expected to be acutely incapacitating and continued flying should not be problematic for patients with symptoms that are well controlled with approved medications. However, when the disease progresses and/or is poorly controlled, the cyclical pain may begin to include non-cyclic pains that can be severe and distracting in an unpredictable pattern. In these cases, more aggressive medical therapy or surgical treatment may be required. A more aggressive therapy, GnRH analogs are administered monthly or every three months depending on the dose, but have persistent effects throughout the dosing period. These medications are often associated with significant and unpredictable side effects that are aeromedically unacceptable. As such, these medications are not aeromedically approved and generally not considered for waiver. A requirement for surgical treatment can be an indicator of the disease severity and failure of medical therapy. Although a history of pelvic surgery is not considered disqualifying when uncomplicated, the severity of the endometriosis of these cases remains disqualifying. Although hysterectomy or removal of one or both ovaries may be therapeutic, removal of both ovaries and uterus is generally considered definitive treatment. In either case, residual or recurrent endometriosis, or an adjuvant treatment

requirement still remain possibilities requiring aeromedical monitoring for possible symptom recurrence. Heavy menstrual bleeding is often associated with endometriosis, and can cause an anemia. Evaluation of the hematocrit and/or hemoglobin levels is necessary in an aeromedical assessment. The primary goal is to treat these patients to the standard of care and the secondary goal is to use a treatment that may be considered for waiver.

Review of AIMWTS through Nov 2018 revealed 50 aviators with an AMS containing the diagnosis of endometriosis: one FC I/IA (disqualified), 14 FC II (5 disqualified), 33 FC III (8 disqualified), one ATC/GBC (not disqualified), and one MOD (not disqualified). Of the 14 cases disqualified, six had symptoms that were not controlled, two were being treated with non-approved medications, one had an inadequate period of observation following surgery, and five had other disqualifying diagnoses.

| ICD-9 code for Endometriosis |                                 |
|------------------------------|---------------------------------|
| 617.9                        | Endometriosis, site unspecified |

| ICD-10 code for Endometriosis |                            |
|-------------------------------|----------------------------|
| N80.9                         | Endometriosis, unspecified |

# **IV. Suggested Readings**

- 1. American College of Obstetricians and Gynecologists. Management of Endometriosis. ACOG Practice Bulletin Number 114, 2010 (Reaffirmed 2018).
- 2. Gorbandt MB and Knittig RA. Women's Health Issues in Aerospace Medicine. In Davis JR, Johnson R, Stepanek J, eds. *Fundamentals of Aerospace Medicine*, 4<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2008:480-490.
- 3. Rayman RB, et al. Ch. 5 in *Rayman's Clinical Aviation Medicine*, 5th Edition, Castle Connolly Graduate Medical Publishing, LTD, 2013; p. 142-43.
- 4. Schenken RS. Endometriosis: Pathogenesis, clinical features, and diagnosis. UpToDate. Online version 49.0. Oct 2018.
- 5. Schrager S, Falleroni J, and Edgoose J. Evaluation and Treatment of Endometriosis. Am Fam Physician, 2013; 87(2): 107-113. https://www.aafp.org/afp/2013/0115/p107.html

#### WAIVER GUIDE

Updated: Mar 2015

Supersedes Waiver Guide of Feb 2012

By: Lt Col Michelle R. Brown (RAM 16) and Dr. Dan Van Syoc Reviewed by Col Pat Storms (RAM 05 and USAF Gastroenterologist)

## **CONDITION:**

**Eosinophilic Esophagitis and Eosinophilic Gastroenteritis Mar 2015**)

## I. Waiver Consideration.

Eosinophilic esophagitis (EoE) or eosinophilic gastroenteritis (EG) is not listed by name specifically in the Medical Standards Directory. Chronic or recurrent esophagitis not controlled by approved medications or with complications including stricture or reactive airway disease is disqualifying for FC I/IA, FC II, FC III, ATC, and SWA duties. Also, symptomatic esophageal disease of any causes is disqualifying for all classes. Therefore, EoE is considered disqualifying for all classes, including GBO duties. It is not waiverable in FCI/IA and unlikely to be waivered in untrained FC II and III candidates. It is potentially waiverable in FC II and III if the individual has no aeromedically significant complications and remains asymptomatic on or off waiverable medications. Gastritis, severe/chronic (confirmed by gastroscopic examination), with repeated symptoms requiring frequent lost duty time is also disqualifying for all classes as well as for retention, and persistent and severe esophagitis is also disqualifying for retention in the US Air Force.

Table 1: Waiver potential for EoE and EG

| Flying Class (FC) | Condition                    | Waiver Potential |
|-------------------|------------------------------|------------------|
|                   |                              | Waiver Authority |
| I/IA              | Eosinophilic esophagitis     | No               |
| Untrained II/III  |                              | AETC             |
|                   |                              |                  |
|                   | Eosinophilic gastroenteritis | No               |
|                   |                              | AETC             |
| II/III            | Eosinophilic esophagitis     | Yes              |
| ATC/GBO/SWA       |                              | MAJCOM           |
|                   |                              |                  |
|                   | Eosinophilic gastroenteritis | Yes              |
|                   |                              | MAJCOM           |

AIMWTS search in Feb 2015 revealed a total of 67 cases with a listed diagnosis of either eosinophilic esophagitis or eosinophilic gastroenteritis. There were a total of 6 disqualifications. Breakdown of the cases was as follows: 5 FC I/IA cases (4 disqualified), 38 FC II cases, 20 FC III cases (2 disqualified), 3 ATC/GBC cases, and 1 MOD case.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for eosinophilic esophagitis or gastroenteritis should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. History with special attention to symptoms, frequency, duration, treatment, precipitating factors, action taken to mitigate recurrence.
- C. Gastroenterology consult evaluation and treatment recommendations.
- D. Endoscopy report.
- E. Pathology report of biopsies of esophagus, antrum and duodenum.
- F. Allergy consult addressing possible food allergies.
- G. MEB results if applicable

The AMS for <u>waiver renewal</u> for eosinophilic esophagitis or gastroenteritis should include the following:

- A. Brief summary of symptoms, treatment, original endoscopy and pathology results and any intervening symptoms or signs (including pertinent negatives e.g. dysphagia, food impaction).
- B. Gastroenterology consult.
- C. Endoscopy report.
- D. Pathology report of biopsies.

#### III. Overview.

The eosinophilic gastrointestinal disorders are comprised of EoE and EG, both which can be seen in adults or children, along with eosinophilic enteritis and colitis. Eosinophils are not distributed homogeneously throughout the gastrointestinal tract. Typically, the highest numbers are found in the cecum and appendix, while the esophageal epithelium is unique in being devoid of eosinophils under normal conditions. Eosinophilic inflammation of the GI tract may represent a primary process or may be secondary to other diseases. The finding of eosinophils in the squamous epithelium of the esophagus is abnormal, according to the American College of Gastroenterology (ACG), who strongly recommends identification of etiology.

Esophageal eosinophils were long thought to be a hallmark of gastroesophageal reflux disease (GERD), but it is now acknowledged that esophageal eosinophilia can appear in response to a variety of stimuli.<sup>3</sup> EoE may be associated with allergy (atopic) or may occur in isolated fashion (idiopathic). Esophageal eosinophilia was first reported in an adult patient in 1975, but it was not until 1995 that unique cases were identified and EoE described as a clinical entity.<sup>4</sup> Despite being a newly recognized entity, it is likely accelerating in incidence.<sup>3</sup> The majority of cases have been in men and occurs in all ages with a peak in the fifth decade of life; the disease can affect all spectrum of age, race or

sex.<sup>5,6</sup> Individual and/or family histories of allergic diseases (food allergies, atopic dermatitis, asthma, allergic rhinitis, allergic conjunctivitis) have been noted in over 50% of individuals with EoE. The most common symptom for EoE is dysphagia to solid food, and esophageal foreign body impaction is now recognized as a major presenting feature of EoE, accounting for over 50% of such episodes.<sup>3,7</sup> Indeed, having EoE was the strongest predictor of having multiple foreign body impactions.<sup>8</sup> Some researchers have pointed to evidence supporting a familial predisposition to EoE which may explain the strong male preponderance.<sup>9,10</sup>

EoE may mimic GERD and can be differentiated from GERD on the basis of the magnitude of mucosal eosinophilia and the lack of response to acid suppression. Some experts feel that EoE and GERD commonly coexist and may be almost indistinguishable from one another. In some cases, the diagnosis was prompted by a poor response to surgical treatment of presumed GERD through fundoplication. Symptoms have usually been present for 4.5 years prior to diagnosis, and are not always associated with a defined esophageal stricture, though proximal strictures in EoE may occur. Endoscopic findings seen with EoE include strictures (frequently proximal), linear furrows, a small-caliber esophagus and multiple white papules (eosinophilic microabscesses). Clinical guidelines for EoE were established in 2013 by the ACG. Diagnostic criteria include both clinical and pathologic information. Esophageal biopsies are required for diagnosis and the ACG strongly recommends two to four biopsies be obtained from both proximal and distal esophagus.

Treatment of EoE is based on limited clinical experience, case series and small controlled trials. The endpoints include resolution of clinical symptom and a reduction in the eosinophilic infiltrate.<sup>2</sup> Acid suppression is usually not successful or at best achieves a partial response. 11 It is, however, commonly used in an effort to combat the pyrosis these patients often report. Systemic or topical corticosteroids have been shown to improve symptoms. Topical steroids, such as fluticasone or budesonide swallowed for eight weeks, are first-line pharmacologic therapy based on strong evidence.<sup>2</sup> Fluticasone is generally administered via metered dose inhaler at a dose of two 220 mcgm puffs swallowed twice daily (880 mcgm/day). Doses as high as 1760 mcgm/day have been used in those refractory to the standard dose. 12 The high relapse rate (~65%) noted in one study in children suggests that chronic or repeated therapy may be needed.<sup>13</sup> There is some evidence for the use of systemic steroids in non-responders to topical steroids and in patients that require rapid improvement in symptoms.<sup>2</sup> Elimination diets and, in particular, elemental diets, have shown improvement in children and adolescents and may be considered as an initial therapy (moderate evidence).<sup>2</sup> Esophageal biopsy and symptom improvement should be used to assess the effectiveness of dietary treatment (recommendation conditional, evidence low).<sup>2</sup>

Dilation of strictures may be initial therapy for individuals with dysphagia and food impaction or used in symptomatic patients with strictures who have failed medical and dietary therapy, but care is warranted, as patients with EoE have delicate esophageal mucosa, prone to tearing, and often have narrowed luminal diameters. <sup>13</sup> Post-dilation substernal pain out of relation to the extent of dilation is commonly encountered in EoE

patients, and repeating EGD after a dilation may reveal long mucosal rents with a very worrisome appearance. No esophageal perforations were reported in one series in which 70 dilations were performed in a group of 36 patients, but post-procedure chest pain and demonstrated mucosal rents warrant a careful approach to dilation in these patients. Antihistamines, cromolyn and montelukast (at doses of about 100 mg/day), and mepolizumab have been used; their efficacy has not been established. Long-term prognosis is unknown. The relatively recent recognition of EoE as a clinical condition has impacted the clear definition of its natural history, but EoE appears to be a chronic disease with a waxing and waning course, as suggested by a noteworthy relapse rate of 80% in an eight-year follow-up of children with EoE, and similarly high rate of recurrent symptoms and chronic therapy in adults.

Eosinophilic infiltration may occur in one or more segments of the GI tract with signs and symptoms related to the layer (mucosa, muscle, and/or subserosa) and extent of bowel involved. In published reports, the stomach (26 to 81%) and small intestine (28 to 100%) are the predominant areas affected.<sup>1</sup> The pathogenesis is not well understood. EG affects 22-28 per 100,000 persons and typically presents with symptoms of abdominal pain, nausea, vomiting, and diarrhea. 15 Endoscopic biopsy is used to confirm eosinophilic infiltration. Symptoms suggesting gastric outlet and intestinal obstruction are common due to a gut made thick and rigid from the eosinophilic infiltration. In subserosal disease, individuals may present with eosinophilic ascites. Peripheral eosinophil counts are elevated in 80% of patients and are frequently seen in mucosal and subserosal disease. 15 EG is associated with atopy manifest as asthma and allergies in 50% of cases. 15 It has a peak onset in the third decade and affects males slightly more than females. 15 Treatment is primarily oral steroids. Cromolyn, montelukast and elimination diets have shown mixed results in published trials. Compliance is of primary concern with elimination diets. The natural history of EG is not well known. Some individuals have no recurrence, while a few will flare concurrently with or immediately after prednisone taper, and still others may experience periodic flares months to years after the initial episode.

#### IV. Aeromedical Concerns.

Symptoms relevant to aviation include dysphagia, food impaction, nausea, vomiting, and chest and/or abdominal pain. The symptoms are of concern primarily due to the potential impact while performing aircrew duties and the effects on mission safety and completion.

Topical corticosteroid therapy, administered via MDI as described earlier, is acceptable for waiver. Montelukast therapy is waiverable, although of uncertain benefit. Approved antihistamines, loratadine (Claritin®) or fexofenadine (Allegra®) and cromolyn are acceptable for waiver. Waiver is not recommended while on systemic steroids. If the individual is asymptomatic after a course of systemic steroids, waiver could be considered after the pituitary axis has returned to normal function (based on Cortrosyn® stimulation testing; see Waiver Guide – Systemic Glucocorticoid [Steroid] Treatment).

| ICD-9-codes for eosinophilic esophagitis and eosinophilic gastroenteritis |   |  |
|---|---|--|
| 530.13  | Eosinophilic esophagitis                              |  |
| 530.19  | Other esophagitis                                     |  |
| 535.70  | Eosinophilic gastritis, without mention of hemorrhage |  |
| 535.71  | Eosinophilic gastritis, with hemorrhage               |  |

| ICD-10-codes for eosinophilic esophagitis and eosinophilic gastroenteritis |   |  |
|--|---|--|
| K20.0  | Eosinophilic esophagitis                  |  |
| K20.8  | Other esophagitis                         |  |
| K52.81   | Eosinophilic gastritis or gastroenteritis |  |

#### V. References.

- 1. Khan S and Orenstein SR. Eosinophilic Disorders of the Gastrointestinal Tract. Ch. 27 in *Feldman: Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 9<sup>th</sup> ed., Saunders, 2010.
- 2. Dellon ES, Gonsalves N, Hirano I, et al. ACG Clinical Guideline: Evidenced Based Approach to the Diagnosis and Management of Esophageal Eosinophilia and Eosinophilia Esophagitis (EoE). Am J Gastroenterol, 2013; 108: 679-92.
- 3. Bonis PAL and Furuta GT. Clinical manifestations and diagnosis of eosinophilic esophagitis. UpToDate. Nov 2014.
- 4. Liacouras CA. Eosinophilic Esophagitis. Gastroenterol Clin N Am, 2008; 37: 989-98.
- 5. Straumann A. Clinical Evaluation of the Adult who has Eosinophilic Esophagitis. Immunol Allergy Clin N Am, 2009; 29: 11-18.
- 6. Almansa C, DeVault KR and Achem SR. A Comprehensive Review of Eosinophilic Esophagitis in Adults. J Clin Gastroenterol, 2011; 45: 658-64.
- 7. Kerlin P, Jones DJ, Remedios, M, et al. Prevalence of Eosinophilic Esophagitis in Adults With Food Bolus Obstruction of the Esophagus. J Clin Gastroenterol, 2007;41: 356-61.
- 8. Sperry SLW, Crockett SD, Miller CB, et al. Esophageal foreign-body impactions; epidemiology, time trends, and the impact of the increasing prevalence of eosinophilic esophagitis. Gastrointestinal Endosc, 2011; 74: 985-91.
- 9. Katzka DA. Eosinophilic esophagitis: it's all in the family. Gastrointest Endosc, 2007; 65(2): 335-36.

- 10. Zink DA, Amin M, Gebara S, and Desai TK. Familial dysphagia and eosinophilia. Gastrointest Endosc, 2007; 65(2): 330-34.
- 11. Baxi S, Gupta SK, Swigonski N, and Fitzgerald JF. Clinical presentation of patients with eosinophilic inflammation of the esophagus. Gastrointest Endosc, 2006; 64(4): 473-78.
- 12. Butz BK, Wen T, Gleich GJ, et al. Efficacy, Dose Reduction, and Resistance to High-Dose Fluticasone in Patients with Eosinophilic Esophagitis. Gastroenterology, 2014; 147:324-33.
- 13. Dellon ES, Gibbs WB, Rubinas TC, et al. Esophageal dilation in eosinophilic esophagitis: safety and predictors of clinical response and complications. Gastroenterol Endosc, 2010; 71(4): 706-12.
- 14. Bonis PAL and Furuta GT. Treatment of eosinophilic esophagitis. UpToDate. Dec 2014.
- 15. Prussin C and Gonsalves N. Eosinophilic gastroenteritis. UpToDate. Aug 2014.

#### WAIVER GUIDE

Updated: Jan 2014

Supersedes Waiver Guide of May 2010

By: Dr Matt Ramage (RAM XV) and Dr Dan Van Syoc

Reviewed by Col Pat Storms, AF RAM and gastroenterologist

## **CONDITION:**

Esophagitis (Jan 2014)

#### I. Waiver Consideration.

Chronic or recurrent esophagitis including reflux esophagitis not controlled by approved medications or that have been complicated by stricture or reactive airway disease is disqualifying for FC I/IA, FC II, FC III, ATC and SWA duties and becomes a retention issue if persistent and severe (requiring repetitive dilatation or dysphagia refractive to treatment). Similarly, esophageal motility disorders not controlled by approved medications are disqualifying. Symptomatic esophageal disease of any causes is also disqualifying for all classes. Therefore, chronic or recurrent esophagitis is considered disqualifying for GBO duties when not controlled by approved medications.

**Table 1: Waiver potential for Esophagitis** 

| Flying Class (FC) | Disease Status                   | Waiver Potential Waiver Authority |
|-------------------|----------------------------------|-----------------------------------|
| I/IA              | Chronic or recurrent             | No                                |
| Initial II/III    | esophagitis                      | AETC                              |
|                   | History of esophagitis, resolved | Maybe<br>AETC                     |
| II/III            | Chronic or recurrent             | Yes                               |
| ATC/GBO/SWA       | esophagitis or history of        | AETC for untrained                |
|                   | esophagitis, resolved            | MAJCOM for trained                |

AIMWTS review in Oct 2013 revealed a total of 936 cases with the diagnosis of esophagitis or an esophagitis-related disorder. There were 11 FC I/IA cases, 443 FC II cases, 0 FC IIU cases, and 417 FC III cases, and 65 ATC/GBC/SMOD cases. Of the total, 16 resulted in a disqualification specifically for esophagitis; 0 cases were FC I/IA, 3 were FC II, 0 were FC IIU, 10 were FC III, and 3 were ATC/GBC/MOD.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for chronic or recurrent esophagitis should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. Thorough discussion of the history and etiology of the condition; detail any prior history of GERD; and list all treatments utilized to include results and side effects.
- C. Consultation report by a gastroenterologist or internist.
- D. Procedure reports: discussion of all endoscopic testing results.
- E. Pathology reports if clinically indicated.

The AMS for <u>waiver renewal</u> for esophagitis should include the following:

- A. Interim history and treatment protocol.
- B. Consultation report by a gastroenterologist or internist.
- C. Procedure reports: discussion of all endoscopic testing results, if applicable.

## III. Overview.

Esophagitis refers to inflammation of the esophageal mucosa. It can be caused by the reflux of gastric contents, infectious organisms, corrosive agents, irradiation, or direct contact with swallowed pills. In looking at the burden of digestive diseases in the US, gastroesophageal reflux disease (GERD) ranks second in prevalence, but is first in annual direct costs.<sup>2</sup> In 2004, 48% of digestive system prescriptions were for GERD; however, this is likely an underestimation as over the counter medication is not included in this calculation.<sup>3</sup> Additionally, in 2004 GERD was listed as causal or first line contributory for 1,150 deaths resulting in 6,000 years potential life lost, and was the leading gastrointestinal ambulatory care diagnosis.<sup>3</sup> In our aviator population, the vast majority of cases will be the result of the progression of GERD to erosive esophagitis (EE). Therefore, the potential impact of esophagitis in the general US population and among our aircrew is substantial. It is estimated that 40% of the U.S. population experiences symptoms of gastroesophageal reflux at least once a month, with 7% experiencing symptoms daily. The integrity of the esophageal mucosa in normal individuals reflects the balance between injurious forces (acid reflux, potency of refluxate) and defensive forces (esophageal acid clearance, mucosal integrity). For one or more reasons, this balance becomes impaired in patients who develop GERD.<sup>4</sup> The prevalence of severe EE increases with age, but the severity of the heartburn symptoms is an unreliable indicator of the severity of erosive disease, particularly in an elderly population.<sup>5</sup>

The mechanisms of GERD and its complications are not completely understood. Most clinicians feel that transient lower esophageal sphincter (LES) relaxation is the key motility disorder in mild to moderate disease. It has been suggested that impaired esophageal clearing of refluxed gastric contents during times of sleep has a significant causative role in reflux esophagitis. In addition, there are indications that esophageal motor dysfunction in patients with reflux esophagitis is a primary phenomenon. There are also some significant racial differences regarding reflux esophagitis and its complications. Barrett's esophagus (BE), a precursor to adenocarcinoma of the esophagus, is more common in non-Hispanic whites than in African Americans. Similarly, heartburn is the primary indication for endoscopy in the non-Hispanic white population, while upper GI bleeding is the primary indication for African Americans.

BE is a complication of GERD and erosive esophagitis and is a premalignant condition. BE can be defined simply as columnar metaplasia of the esophagus and is seen in 8% to 20% of patients with chronic GERD. Many gastroenterologists feel that the major reason to evaluate a patient with longstanding GERD is to be able to recognize BE. The overall incidence of BE in the general population is difficult to estimate as approximately 25% of BE patients have no symptoms of reflux. One multi-center study demonstrated that the prevalence of BE was 6.8% in evaluation of patients with or without the symptoms of heartburn, and rose to 15% if they had erosive esophagitis on endoscopy. Epidemiologic data also indicate that men are at greatest risk and, although Barrett's esophagus can be found at any age, the prevalence increases with advancing age until a plateau is reached in the 60s. While there is insufficient evidence of morbidity or mortality benefit, of those who received endoscopic evaluation for the indication of chronic GERD, 3-15% were found to have BE. 9-12

Dyspeptic substernal distress may reflect conditions other than GERD. Physical examination, laboratory testing, and radiographic imaging aid in the exclusion of alternate diagnoses. Chief among diseases to be excluded are coronary artery disease, gallbladder disease, peptic ulcer disease and pill esophagitis. In the simplest case, when symptoms are typical and the patient responds to therapy intended to address those symptoms, no diagnostic tests are required. Rather, diagnostic testing is invoked in 3 broad scenarios: (1) to avoid misdiagnosis, (2) to identify complications of reflux disease, and (3) in the evaluation of empirical treatment failures." The concept of alarm features is commonly cited as a screening mechanism to decide whether diagnostic tests are necessary. "Alarm features include, evidence of gastrointestinal blood loss, involuntary weight loss, dysphagia.<sup>13</sup>

Proton pump inhibitors (PPIs) are considered the most effective short-term treatment for GERD. PPIs are well tolerated, with headaches and diarrhea described as the most common side effects. Histamine-2 Receptor Antagonists (H2RAs) have also long been used effectively to treat symptoms of GERD and reflux esophagitis. They tend to be less successful than are the PPIs in more severe disease states with healing rates rarely exceeding 60% after up to 12 weeks of treatment. The dosage of the H2RA agents often has to be significantly increased to approach healing rates of the PPIs, and PPIs generally provide better symptom control and better mucosal healing. There is an increased risk of hip fractures with long term use of PPIs when compared to H2RA and nonusers of secretion inhibitors alike over the age of 50. The risk of fracture increases with increased cumulative duration of PPI exposure.<sup>14</sup> As ubiquitous as PPIs are, they should not be employed without careful consideration of risk versus benefit for the individual patient. Prokinetics, such as bethanechol, a cholinergic agonist; metoclopramide, a dopamine antagonist; and cisapride, a serotonin (5-HT4) receptor agonist that increases acetylcholine release in the myenteric plexus, have been used in the past in treatment of GERD, but have fallen out of favor, or are no longer available. These drugs improve reflux symptoms by increasing LES pressure, acid clearance, and/or gastric emptying. While these agents provide modest benefit in controlling heartburn, they are unreliable in healing esophagitis unless combined with acid inhibiting drugs. Prokinetic drugs are also significantly limited by their side-effect profiles. 15-17 Sucralfate, an aluminum sucrose polysulfate, potentiates

cytoprotection and mucosal resistance and is safe to use in initial and maintenance therapy, though its efficacy is limited in treating GERD symptoms. Some patients with significant GERD and erosive esophagitis may need to consider surgical solutions such as the laparoscopic Nissen fundoplication procedure.

Medication-induced esophagitis is an increasing problem in our country. The types of medications causing direct esophageal injury can be divided into antibiotics, anti-inflammatory agents and others. Tetracyclines are the most common antibiotic to induce esophagitis, particularly doxycycline. Taking tetracycline with a full glass of water, and avoiding a recumbent posture for several hours after taking the medication provides the best opportunity to avoid esophageal injury. All of the currently used anti-inflammatory agents can damage the esophagus, with the highest number of reported cases with aspirin. The flight surgeon also needs to be aware of problems with nutritional supplements. A recent surge in the use of compounds such as NANO<sup>X9</sup> has led to increased esophagitis symptoms in military members (anecdotal story), impacting seven members in one deployed location. The mechanism of injury is believed to be due to prolonged contact of the caustic contents of the medication with the esophageal mucosa. Most cases of medication-induced esophageal injury heal without intervention within a few days. Thus, the most important aspect of therapy is to make the correct diagnosis and then to avoid reinjury with the agent.<sup>18</sup>

## IV. Aeromedical Concerns.

Increases in intra-abdominal pressure, changes in gravitational position, and abdominal muscle contraction all increase the pressure gradient between the abdomen and the thorax, worsening GERD and potentially inducing GERD symptoms. Furthermore, with the increasing prevalence of obesity in the general population, a similar trend is seen in the aviator population. A 2009 meta-analysis shows that there is an increased risk of BE in patients with a BMI ≥30 compared to those with a BMI <30.19 Reflux symptoms are of aeromedical concern because they can distract the aircrew member, though they are normally not disabling. The symptoms can be potentially disabling if the aviator has intractable coughing and aspirates, this is of major concern in the high-performance cockpit in which there are little to no crew redundancies. The availability of OTC medications can mask symptoms of severe disease until the flyer presents with significant medical complications like hemorrhage or stricture. Acute hemorrhage secondary to mucosal ulcers may occur in aircrew with chronic GERD and severe esophagitis, and can be disabling. Acute esophageal obstruction, caused by food impaction in the face of a peptic stricture, can also be disabling. In addition, medications used to control esophagitis may cause disqualifying side effects. The prokinetic agents metoclopramide and cisapride are not compatible with flying duties and should not be used as first line agents. Typical antacids are safe to use in an aeromedical environment, but their use may be a marker of worsening or breakthrough symptoms. Members requiring frequent antacids may warrant more aggressive care. Some H<sub>2</sub>-receptor antagonists and PPIs are well-tolerated and recent changes to the Approved Aircrew Medication list have removed the necessity of a waiver if certain medications are well tolerated and control symptoms. At this time, the current approved GERD and EE medications are esomeprazole (Nexium®), omeprazole

(Prilosec®), rabeprazole (Aciphex®), lansoprazole (Prevacid®), ranitidine (Zantac®), cimetidine (Tagamet®), famotidine (Pepcid®), pantoprazole (Protonix®), and sucralfate (Carafate®). Each can be used to treat GERD or EE after a three day grounding period to rule out idiosyncratic reaction and to assure symptoms are controlled (See Official Air Force Approved Aircrew Medication list). Finally, for those aviators with Barrett's esophagus, there is concern regarding the future risk of esophageal cancer. The incidence of Barrett's esophagus progressing to adenocarcinoma is estimated to be 0.5 per 100 patient-years (i.e., one in 200 patients developing carcinoma per year). As adenocarcinoma of the esophagus is a devastating disease, BE patients need to be followed closely.

| ICD-9 codes for esophagitis |                            |  |
|-----------------------------|----------------------------|--|
| 530.10                      | Esophagitis, unspecified   |  |
| 530.11                      | Reflux esophagitis         |  |
| 530.12                      | Acute esophagitis          |  |
| 530.19                      | Other esophagitis          |  |
| 530.2                       | Ulcerative esophagitis     |  |
| 530.3                       | Esophageal stricture       |  |
| 530.82                      | Esophageal hemorrhage      |  |
| 530.85                      | Barrett's esophagitis      |  |
| 530.89                      | Other esophageal disorders |  |

| ICD-10 codes for esophagitis |   |
|------------------------------|---|
| K20.9                        | Esophagitis, unspecified                  |
| K21.0                        | Gastro-esophageal reflux with esophagitis |
| K20.8                        | Other esophagitis                         |

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#### WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of Aug 2013

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#### **CONDITION:**

**Eustachian Tube Dysfunction (Jan 2018)** 

## I. Waiver Consideration.

Acute Eustachian tube dysfunction (ETD) secondary to a transient illness (e.g. viral URI or SAR) requires no waiver but is grounding for flyers until resolution. However, chronic ETD is disqualifying (MSD D6) and requires a waiver for FC I/A, FC II, FC III, OSF, and SWA duties. Also any surgical procedure for correction of ETD (MSD D7) is disqualifying for FC I/A, FC II, FC III, OSF, and SWA duties. It needs to be emphasized that resolution of ETD and adequacy of ET function are to be assessed on a case by case basis and that no one treatment or procedure, per se, will lead to waiver approval. Regardless of cause or treatment modality, ET functionality must be demonstrable for a waiver to be granted. In general, the permanent use of PE tubes in flyers is not advisable, but it is a fact that adults tend to tolerate chronic use of PE tubes better than children. What is important is the operational necessity of using the tubes and the clinical judgment of the flight surgeon and treating otolaryngologist.

For GBO and ATC personnel, ETD is not listed specifically as disqualifying. However, per AFI 48-123 on general and miscellaneous conditions and defects, retention standards are in play when satisfactory performance of duty is prevented or there is a requirement for extensive and prolonged treatment. If these conditions exist, the member will need a waiver if returned to duty after MEB.

**Table 1: Waiver potential for ETD** 

| Flying Class (FC) | Condition                    | Waiver Potential |
|-------------------|------------------------------|------------------|
|                   |                              | Waiver Authority |
| I/IA              | ETD/OM, regardless of        | Maybe*           |
|                   | cause, controlled with nasal | AETC             |
|                   | steroids and/or approved     |                  |
|                   | oral antihistamines.         |                  |
|                   |                              |                  |
|                   | ETD/OM, regardless of        | Maybe*#          |
|                   | cause, controlled via        | AETC             |
|                   | surgical correction.         |                  |
| II/III            | ETD/OM, regardless of        | Yes*             |
| SWA               | cause, controlled with nasal | MAJCOM           |
|                   | steroids and/or approved     |                  |
|                   | oral antihistamines.         |                  |
|                   |                              |                  |
|                   | ETD/OM, regardless of        | Yes*#            |
|                   | cause, controlled via        | MAJCOM           |
|                   | surgical correction.         |                  |
| ATC/GBO           | ETD/OM, regardless of        | N/A              |
|                   | cause.                       |                  |

<sup>\*</sup> Waiver in FC I/IA and untrained FC II/III requires at least 12 months of symptoms controlled on medication before waiver.

A review of AIMWTS through Jan 2018 revealed 207 cases with the diagnosis of ETD with 117 cases disqualified. Breakdown of the cases was as follows: 6 FC I/IA cases (4 disqualified), 50 FC II cases (17 disqualified), 135 FC III cases (94 disqualified), 8 RPA Pilot cases (0 disqualified), 7 ATC/GBC cases (2 disqualified), and 1 MOD case (0 disqualified). In every case, except two (optic drusen and migraines), the disqualifying diagnosis was the ETD/inadequate or absent Valsalva. In almost every case where the ETD was treated with aeromedically waiverable medications and/or surgical correction (e.g. PET, adenoidectomy, cholesteatoma resection, nasal polypectomy, etc.), the waiver was granted in the presence of subsequently demonstrated pressure equalization (e.g. altitude chamber). In only one case was a granted waiver subsequently denied due to recurrent ETD.

<sup>#</sup> Waiver may be considered if at least 6 months after surgery, symptoms entirely resolved, clearance by ENT physician. ENT clearance is mandatory as different surgical procedures (e.g. PET vs. cholesteatoma resection) have dramatically different recovery periods and associated complications. Further, any surgical complications (e.g. hearing loss) require evaluation and waiver of their own accord.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for initial waiver for ETD should include the following:

- A. History symptoms (flying and on ground), duration, and treatment.
- B. Physical HEENT including Valsalva.
- C. ENT consultation report to include any surgical reports if applicable.
- D. Audiology with Impedance test consultation report.
- E. Altitude chamber flight results (Altitude chamber ride up to 8-10,000ft with rapid decompression is required. If treated with surgery, altitude chamber ride no earlier than 6 weeks after surgery or when cleared by ENT physician, whichever is later). This only applies to those whose duties are at altitude

The AMS for <u>waiver renewal</u> for ETD and/or surgery should include the following:

- A. History interim summary of any symptoms (flying and on ground), treatments, or recurrences/exacerbations since last waiver.
- B. Physical HEENT including Valsalva.
- C. ENT consultation if symptoms recurrent.
- D. Audiology consult if symptoms recurrent.
- E. Status report of ET functional capacity in flight (i.e. any in-flight symptoms?).

## III. Overview.

Eustachian tube dysfunction (ETD), which is most easily recognized as difficulty clearing one's ears, is often the cause for grounding of airmen. While most occupations require only normal hearing, a normal otoscopic exam, and absence of an ear disease history, the requirements for flight duty are far more rigorous. Sudden changes in atmospheric pressure, as are often experienced by aviators, demand tubal equilibrating capacity to be in optimal working order. Failure to equilibrate to rapid changes in atmospheric pressure can lead to the sudden onset of "ear block" – (barotrauma resulting in severe ear pain due to the inability to equilibrate pressures in the middle ear). This sudden onset of severe pain may be incapacitating and pose great risk to safety of flight.

Our knowledge and understanding of the functions and diseases of the eustachian tubes (ET) are due to the pioneering works of men such as Bartolomeus Eustachius (16<sup>th</sup> century anatomist), Antonio Valsalva (18<sup>th</sup> century anatomist), and Adam Politzer (19<sup>th</sup> century otologist). As an outgrowth of their endeavors, we now realize that the ET serves three physiologic functions: 1) pressure regulation, 2) protection of the middle ear from pathogens/foreign material in the nasopharynx, and 3) clearance of the middle ear space.<sup>3</sup> Failure of the tubal mechanism can disrupt any and/or all of these functions. This altered tubal function may then lead to a multitude of complications which vary from mild and transient (i.e. causing temporary DNIF) to severe and debilitating (i.e. permanently disqualifying). For example, the transient difficulty clearing ears caused by viral upper

respiratory tract infections (URIs) and/or seasonal allergic rhinitis (SAR) may only cause mild and/or fleeting symptoms. However, ETD has also been linked to the development of chronic otitis media and secondary cholesteatoma (trapping of squamous debris in the middle ear and mastoid).

In its resting state, the ET remains closed and only opens when necessary to equalize pressure. In flight, ascent usually causes little trouble even in the absence of any active ear clearing maneuvers. This is due to the passive escape from the middle ear of expanding air as it exceeds the opening pressure of the ET. However, 10-17% of airmen have reported vertigo during ascent which is believed to be secondary to asymmetry between the right and left side (i.e. alternobaric vertigo-causing a differential input to the vestibular system).<sup>1,2</sup> This is more frequently seen on descent which requires the active passage of air into the middle ear space. This is normally accomplished by the tubal musculature associated with deglutition and/or jaw movements. The most well-known example of this is the *Toynbee's maneuver*: displacement of air by the movement of the eardrum when swallowing with the nose closed. Should such maneuvers fail, air can be forced into the middle ear by increasing nasopharyngeal pressures via the Valsalva maneuver: displacement of air by the movement of the eardrum caused by forceful expiration against a closed nose.<sup>4</sup> Many authorities suggest as safer alternatives the Toynbee or Frenzel maneuvers: open the jaw, fill mouth with air, pinch the nose, purse the lips, and then close the jaw while displacing air posteriorly by pushing the tongue up and back.<sup>4</sup> In a minority of cases, anatomic, hormonal, and disease factors cause the ET to be remain open continuously (i.e. a patulous ET). This often leads to auditory complaints including autophony (hearing one's own breathing).

There are myriad etiologies of ETD and not all are understood in their entirety. Many mechanisms are easily understood. For example, the initiation of swelling, inflammation and/or drainage within the ET caused by entities such as viral URI, chronic sinusitis, and/or allergic rhinitis is a rather straightforward cause. Further, obstructive mechanisms such as adenoid hypertrophy, deviated nasal septum, or nasal polyposis are also well known. Less well appreciated, however, are other causes of ETD such as the decreased tubal function associated with tobacco smoke (decreased ciliary function), reflux disease (nasopharyngeal exposure to gastric contents), and congenital abnormalities (location/angle of tube, cleft palate, reduced mastoid air cell system).<sup>3</sup> It is now felt that there are three subtypes of ETD: dilatory, baro-challenge induced, and patulous.<sup>5</sup>

Any history of fullness or clogging of the ears, otalgia, hearing loss, tinnitus or dizziness should prompt an evaluation for ETD. A common complaint is that no amount of yawning, swallowing, chewing or attempted Valsalva maneuver alleviates the symptoms. Several methods are available to assess the function of the ET in the office. Otoscopic observation of tympanic membrane (TM) mobility caused by the Toynbee, Frenzel, Valsalva maneuvers and/or pneumatic otoscopy is good evidence of a functional/patent ET. Likewise, a normal tympanogram attests to the normal transmission of energy through the middle ear space.<sup>3</sup> However, studies have not shown good correlation between a normal tympanogram and any predictive value for barotrauma.<sup>2</sup> The 7-Item Eustachian Tube Dysfunction Questionnaire (ETDQ-7) was designed by McCoul et al. as

a disease-specific instrument for the assessment of symptoms related to obstructive dysfunction of ET.<sup>6</sup> This validated questionnaire can be helpful in assessing the degree of ETD as well as treatment response. The limiting factor for all of these assessment tools; however, is that none of them assess ET function during the dynamic changes in atmospheric pressure experienced by aviators. However, the ETDQ-7 has shown to discriminate between patients with baro-challenge-induced ET dysfunction and healthy controls and may be helpful in the aeromedical community.<sup>7</sup> Such complex function should be tested during simulated flights in a pressure chamber.<sup>1</sup> Even this assessment, however, short of expensive and invasive pressure manometer placement, is dependent upon the subjective report of the aviator. Seeking the best combination of cost, non-invasiveness and accurate surrogacy for the dynamic flight environment has led the USAF to select demonstration of a normal Valsalva maneuver and successful completion of a pressure chamber flight as criteria for pilot selection and training.<sup>1</sup> The main predictors of barotrauma continue to be a previous history of nasal or otologic disease and/or abnormal otoscopy.<sup>2</sup>

Treatment of ETD should be directed at the underlying etiology, if known, as well as any resultant complications.<sup>8</sup> Review of the medical literature reveals no clear consensus on the efficacy of common treatment modalities for ETD.<sup>9</sup> While there are studies showing promising results from treating inflammatory, congestive and allergic causes for ETD with the appropriate oral/topical decongestant, antihistamine or nasal steroid, there are also studies which do not duplicate such promising outcomes. 10-13 Likewise, success rates following surgical correction for ETD have varied. Insertion of pressure equalization tubes (PET) has long been the mainstay of surgical treatment for ETD. However, several investigators have found that while the pressure differential between the middle ear and the external auditory canal may be immediately resolved, the function of the ET itself does not change following PET insertion. Other procedures such as adenoid resection and laser eustachian tuboplasty have also shown a mix of success and failure in treating ETD.<sup>3</sup> Thus, regardless of whether medically or surgically treated, and regardless of specific etiology, the outcome of any treatment for ETD needs to be evaluated on a case by case basis to determine the presence of acceptable ET function. This is especially true in the aviator population.

Recently, balloon dilation of the cartilaginous ET (BDET) has shown encouraging results and was approved by the FDA for use in 2016. Published results have shown that BDET can effectively improve ET function in ears with ETD, OME or atelectasis. <sup>14-16</sup> The procedure, which usually requires general anesthesia in the OR, is generally well tolerated and without significant complications. International studies on BDET demonstrated to be effective in 70% of a large cohort of patients affected by obstructive ET dysfunction. <sup>14, 15</sup> In a prospective study with moderately long-term follow-up, it showed significant improvement in aeration of the middle ear and ability to perform a Valsalva maneuver. Patients with presumably irreversible disease, but having had their underlying etiology adequately managed, appear to be candidates for the procedure and it is now commonly performed in military treatment facilities by ENT surgeons/otologists. <sup>16</sup>

ETD and otitis media (OM), another common disorder of the middle ear, are closely related. Historically, the pathophysiology of OM has always been linked with abnormalities of ET function. As previously reviewed, the ET performs the three classic functions of aeration, clearance, and protection of the middle ear. Traditional teaching has held that the ET function of aeration was limited and that this was the underlying cause of most acute otitis media (AOM). More recent investigation, however, has suggested that AOM is the result of bacterial entry into the middle ear (i.e., failure of protection). In either case, that there is a relationship between ETD and the development of OM is clear. Whether or not ETD precedes AOM, the finding of ETD in patients with AOM is nearly universal.<sup>17</sup> While space here does not permit a separate treatise on OM and its many variants, the following five principles derived cooperatively by the Centers for Disease Control and the American Academy of Pediatrics should help to guide OM-related diagnosis and treatment decisions: 1) the diagnosis of OM should not be made unless fluid is present in the middle ear, 2) OM should be classified as AOM or otitis media with effusion (OME) on the basis of the presence or absence of signs and symptoms of acute illness, 3) in contrast to AOM, OME should not be treated with an antibiotic, 4) effusion is likely to persist after the treatment of AOM and does not require repeated treatment, and 5) antibiotic prophylaxis for AOM should be used only in accordance with strict criteria. 18

For questions regarding the complication of cholesteatoma, please refer to the waiver guide on that topic.

#### IV. Aeromedical Concerns.

ETD may result in the failure to equilibrate middle ear pressures and lead to pain, impairment of hearing, and vertigo, with or without rupture of the tympanic membrane, resulting in compromised aircraft safety if a member of the crew is incapacitated in this way. ETD may only be minimally symptomatic at ground level. However, such tubal dysfunction can block the flow of air in and out of the middle ear space. In the presence of ETD, dynamic perturbations of atmospheric pressure may result in acute barotrauma, resulting in sudden, incapacitating pain. Should such an event occur immediately prior to or during landing procedures, it could lead to sudden incapacitation and an aircraft mishap. Treatment should consist of returning to altitude to allow slower equilibration of the middle ear, the use of oxymetazoline nasal spray (Afrin®), and if the block persists on landing, the use of a Politzer bag to assist in ventilating the middle ear. Aviators need to take caution with the use of such nasal sprays. Overuse can lead to inhibition of normal smooth muscular tonality of the vascular nasal mucosa, leading to rhinitis medicamentosa, which results in mucosal swelling and secretions; the exact opposite of the desired outcome.

There is no quick test to ensure the ET is patent prior to flight; but, being free of sinonasal and URI symptoms and being able to Valsalva and prior successful completion of altitude chamber training are a close approximation. Further, any middle ear disturbance (e.g. ETD or OM) raises concern for decreased and/or loss of hearing, disequilibrium, and the development of more extensive disease.

There are some concerns about the chronic use of PE tubes in aviators. Most patients requiring prolonged PE tubes will end up with a large central perforation which tends to remain as long as the ear is not being ventilated. Also, the PE tubes can fail. They get plugged, extrude, cause granulation tissue which then causes bleeding and infection, and can cause perforations of the TM. They can also act as a conduit for fluids getting in the middle ear especially soapy fluids with low surface tensions that then can cause a chemical irritation of the middle ear and subsequent otorrhea/infection. The other challenge is that it sometimes takes a microscope and other specialized otologic instrumentation to accurately evaluate and mediate PE tube problems, so a deployed FS evaluating with an otoscope may not be able to discern what is happening with the tube or TM.

| ICD-9 codes for Eustachian Tube Dysfunction and Otitis Media |  |  |
|--|--|--|
| 381.5  | Eustachian salpingitis                 |  |
| 381.6  | Obstruction of the Eustachian tube     |  |
| 381.7  | Patulous Eustachian tube               |  |
| 381.8  | Other disorders of the Eustachian tube |  |
| 381.9  | Unspecified Eustachian tube disorder   |  |

| ICD-10 codes for Eustachian Tube Dysfunction and Otitis Media |   |  |
|---|---|--|
| H68.00  | Unspecified Eustachian salpingitis, right ear, left, bilateral, unspecified |  |
| 1, 2, 3, 9  | ear   |  |
| H68.10  | Unspecified obstruction of the Eustachian tube, right ear, left, bilateral, |  |
| 1, 2, 3, 9  | unspecified ear   |  |
| H69.0   | Patulous Eustachian tube, unspecified ear, right, left, bilateral           |  |
| 0, 1, 2, 3  |   |  |
| H69.8   | Other specified disorders of the Eustachian tube, unspecified ear, right,   |  |
| 0, 1, 2, 3  | left, bilateral   |  |
| H69.9   | Unspecified Eustachian tube disorder, unspecified ear, right, left,         |  |
| 0, 1, 2, 3  | bilateral   |  |

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#### WAIVER GUIDE

Updated: Feb 2017

Supersedes Waiver Guide of Jul 2013

By: Lt Col Elizabeth Casstevens (RAM 18) and Dr. Dan Van Syoc

Reviewed by Col Pat Storms, RAM 05 and AF/SG consultant for gastroenterology

## **CONDITION:**

Gastroesphageal Reflux Disease (Feb 2017)

## I. Waiver Considerations.

According to the Medical Standards Directory (MSD), symptomatic esophageal disease, chronic or recurrent esophagitis, Gastroesophageal Reflux Disease (GERD), or esophageal motility disorders, not controlled by medications listed in the AF Approved Medications guide or with complications including stricture or reactive airway disease is disqualifying for all flying classes, ATC/GBO, and SWA personnel. If GERD symptoms are controlled by approved medications, a waiver is not required. The current approved GERD medications are esomeprazole (Nexium®), omeprazole (Prilosec®), rabeprazole (Aciphex®), lansoprazole (Prevacid®), ranitidine (Zantac®), cimetidine (Tagamet®), famotidine (Pepcid®) or pantoprazole (Protonix®). Each can be used to treat GERD after a three day grounding period to rule out idiosyncratic reaction and to assure control of symptoms. Eosinophilic esophagitis is an entity outside of GERD, and should be separately considered (if applicable, see Waiver Guide for eosinophilic esophagitis). Consultation with a gastroenterologist is recommended in patients with eosinophilic esophagitis.

**Table 1: Waiver Potential for GERD** 

| Flying Class (FC) | GERD Status                        | Waiver Potential    |
|-------------------|------------------------------------|---------------------|
|                   |                                    | Waiver Authority    |
| I/IA              | Uncomplicated GERD                 | Waiver not required |
|                   | controlled by approved             |                     |
|                   | medications                        | Yes                 |
|                   |                                    | AETC                |
|                   | GERD controlled by Surgery*        |                     |
|                   |                                    | No                  |
|                   | GERD not controlled by             | AETC                |
|                   | approved medications or            |                     |
| TT /TTT           | surgery                            | ***                 |
| II/III            | Uncomplicated GERD                 | Waiver not required |
|                   | controlled by approved medications |                     |
|                   | medications                        | Yes                 |
|                   | GERD controlled by Surgery*        | MAJCOM              |
|                   | GERD controlled by Surgery         | MAJCOM              |
|                   |                                    | Maybe               |
|                   | GERD not controlled by             | MAJCOM              |
|                   | approved medications or            |                     |
|                   | surgery#                           |                     |
| ATC/GBO           | Uncomplicated GERD                 | Waiver not required |
| SWA               | controlled by approved             |                     |
|                   | medications                        |                     |
|                   |                                    | Yes                 |
|                   | GERD controlled by Surgery*        | MAJCOM              |
|                   |                                    | Maybe               |
|                   | GERD not controlled by             | MAJCOM              |
|                   | approved medications or            |                     |
|                   | surgery#                           |                     |

<sup>\*</sup> If surgery is successful and patient does not require maintenance medications, no waiver is necessary. A waiver will be required if medication usage is still required, even for medications on the approved list. # Unapproved medications <u>may</u> be considered on a case-by-case basis after discussion with waiver authority and the ACS. This consideration is typically done only after failure on an adequate trial of all approved medications, and even then approval is not guaranteed.

AIMWTS review in November 2016 revealed 2285 aircrew with an AMS for GERD, 175 were disqualified. Breakdown by flying class includes: FC I/IA – 31 cases (13 DQ), FC II – 1115 cases (48 DQ), FC III – 992 cases (91 DQ), ATC/GBC – 114 cases (17 DQ), MOD – 31 cases (1 DQ). As evidenced, over 90% of these cases received a waiver and almost every disqualification was due to a diagnosis other than GERD.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for GERD should include the following:

- A. History of symptoms and all treatments attempted, with response to each treatment.
- B. Diagnostic test results and findings.
- C. Consultation from treating physician.
- D. Documentation of resolution of symptoms and observation for adverse reaction.

The AMS for <u>waiver renewal</u> for GERD should include the following:

- A. Interval history since last waiver submission.
- B. All applicable labs and imaging tests as in the initial aeromedical summary.
- C. Consultation from treating physician.

## III. Overview.

The Montreal Classification defines GERD as "a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications." About 40% of US adults complain of monthly heartburn, about 20% complain of weekly heartburn, and about 7% complain of daily heartburn.<sup>2</sup> The most common symptoms of GERD are pyrosis, regurgitation, and dysphagia. Other symptoms may include odynophagia, water brash, chest pain, globus sensation, nausea, and hemorrhage. Pulmonary symptoms may be the only clinical manifestations of gastroesophageal reflux (GER) and include chronic cough, wheezing, asthma, hemoptysis, hoarseness and recurrent aspiration pneumonia.<sup>3</sup> The pathophysiology of GER reflects a multifactorial process, though inappropriate transient lower esophageal sphincter (LES) relaxation is thought to be the key motility disorder in mild to moderate disease. The primary difference between GER (or episodic heartburn) and GERD hinges on the word "troublesome" in the above Montreal Classification; functional or episodic heartburn in the absence of esophageal injury, and which does not occur at a high enough frequency or severity to be perceived as "troublesome" to the member, does not meet the definition of GERD.<sup>4</sup> As such, the member is unlikely to seek treatment for their condition. The diagnosis of GERD can be made by a history indicating any of the symptoms previously mentioned. When indicated based on risk factors, co-existent symptoms, or prior history of esophagitis, severity of mucosal damage and complications of reflux esophagitis can be assessed through endoscopy. Endoscopy may be normal in many patients with GERD (up to 40%) or may reveal erosions, ulceration, peptic stricture, mucosal changes suggesting a columnar celllined lower esophagus (Barrett's esophagus), or adenocarcinoma. In addition, eosinophilic esophagitis commonly presents with dyspeptic symptoms or dysphagia, and may demonstrate endoscopic evidence of "trachealization" of the esophageal mucosa.<sup>5</sup> The presence of alarm symptoms, such as dysphagia, weight loss, and bleeding, suggest more complicated disease and warrant endoscopic investigation.<sup>6</sup> The differential diagnosis of GERD includes peptic ulcer disease, gastritis, symptomatic gallstones, and

non-steroidal anti-inflammatory (NSAID)-induced GERD, and eosinophilic esophagitis, all of which should be at least briefly considered in the dyspeptic patient. Mildly symptomatic cases could benefit from lifestyle changes prior to pharmacologic interventions. Additional conservative treatment measures include the avoidance of fatty foods, chocolate, and carminatives (spearmint, peppermint). Patients should also be taught to avoid wearing tight clothing, eating large meals, and reclining soon after eating. Obesity is strongly correlated to GER through a variety of mechanisms, and should be a focus of non-pharmacologic intervention. Alcohol and smoking can decrease LES pressure and/or delay gastric emptying which can cause/worsen symptoms of GER.

Most individuals with either heartburn or regurgitation, will self-medicate with OTC H<sub>2</sub>receptor antagonist regimens (ranitidine or famotidine), or proton pump inhibitors (PPIs) such as Prilosec OTC. The current consensus is that empiric therapy is appropriate initial management for patients with uncomplicated heartburn.<sup>7</sup> Patients whose heartburn has not adequately responded to twice daily PPI therapy should be considered treatment failures, making that a reasonable upper limit for empiric therapy.<sup>8</sup> Note that empiric therapy is appropriate only for "uncomplicated" dyspeptic symptoms. Patients with alarm symptoms such as GI bleeding, unexplained weight loss, or dysphagia should be considered for endoscopic assessment rather than empiric therapy. It is critical to note that atypical chest pain could be a manifestation of symptomatic coronary artery disease or other significant extra-esophageal pathology; as such, one should always consider atypical presentations of significant non-gastrointestinal disease before starting a regimen of empiric therapy. Endoscopy is indicated for patients whose symptoms fail to respond to twice daily PPIs. Assessment of patients with persistent dyspeptic symptoms, no response to empiric PPIs, and a normal endoscopy is beyond the scope of this waiver guide and referral of these patients to a gastroenterologist is recommended.

PPIs remain the pharmacologic mainstay for treatment of GERD, but other treatments may be considered in patients with demonstrated esophagitis and an inadequate response to PPIs. Prokinetic agents such as metoclopramide may enhance gastric emptying and reduce reflux episodes, but are not waiverable secondary to their side effect profile. In refractory cases of GERD, antireflux surgery may be considered. Nissen fundoplication, the preferred antireflux procedure, reinforces the lower esophageal sphincter with a 360-degree gastric wrap around the lower esophagus. Nissen procedures are routinely performed through laparoscopy or thoracoscopy. It is important to rule out contraindications of a Nissen, such as esophageal dysmotility, prior to considering this treatment option. Complications of GERD include esophageal strictures, ulceration with or without hemorrhage, and the development of Barrett's esophagus. Any of these complications should prompt referral to a gastroenterologist for further evaluation and treatment.

## IV. Aeromedical Concerns.

Increases in intra-abdominal pressure, changes in gravitational position, and abdominal muscle contraction all increase the pressure gradient between the abdomen and the thorax, potentially worsening GERD and its attendant symptoms. These changes are of major

concern in the high-performance cockpit. Reflux symptoms are of aeromedical concern because they can distract the aircrew member even if the symptoms are not disabling. The availability of OTC medications can mask symptoms of severe disease until the flyer presents with significant medical complications like hemorrhage or stricture. Inadequately treated GERD has a high rate of recurrence, which can be very troubling for the aviator. Acute hemorrhage secondary to mucosal ulcers can occur in aircrew with chronic GERD and severe esophagitis, and can be disabling. Acute esophageal obstruction, caused by food impaction in the face of a peptic stricture, can also be disabling. A more subtle impact of GERD on flying performance is reflected in a recent review, suggesting that GERD could disturb sleep by causing difficulty in falling asleep, sleep fragmentation caused by short amnestic arousals, and/or conscious awakenings, and awakenings in the early morning. 11

As already noted, medications used to control GERD may cause disqualifying side effects. Metoclopramide, a dopamine antagonist, crosses the blood-brain barrier. Up to 20% of patients experience psychotropic side effects which include somnolence, lassitude, restlessness, anxiety, insomnia, and rarely extrapyramidal reactions. Sucralfate, an aluminum sucrose polysulfate, potentiates cytoprotection and mucosal resistance. It is safe to use in initial and maintenance therapy, though its efficacy is limited in symptomatic GERD. Antacids are also safe to use in an aeromedical environment, but can cause diarrhea if used in sufficient doses to positively impact chronic GERD symptoms.

| ICD-9 code for GERD |                   |  |
|---------------------|-------------------|--|
| 530.81              | Esophageal reflux |  |

| ICD-10 code for GERD |  |  |
|----------------------|--|--|
| K21.9                | Gastro-esophageal reflux disease without |  |
|                      | esophagitis                              |  |

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# Glaucoma and Ocular Hypertension (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Michael Parsons (Deputy Chief, Aerospace Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: New Ground Based Operator (GBO) Standards. MSD C6, C7, C8.

## I. Waiver Consideration

Glaucoma is disqualifying for all flying classes (except GBO and OSF), and for retention. There is no waiver potential for *initial* aircrew applicants. Glaucoma is most simply defined as an acquired and progressive optic neuropathy, often associated with raised intraocular pressure over time. However, glaucoma is disqualifying for all flying classes including GBO and OSF duties if there are demonstrable changes in the optic disc or visual fields or if the condition is not amenable to treatment. Additionally, initial GBO and OSF applicants with the diagnosis of glaucoma who do not meet the retention standard (only C7 applies) will require a waiver to commission or access into the Air Force prior to flying or special operational duty consideration. The waiver authority for those cases is the Air Education and Training Command (AETC) and each applicant will be considered on a case-by-case basis.

Glaucoma in trained aircrew (all flying classes) is potentially waiverable, provided the following conditions are met. First, that there is stable glaucoma controlled by medications or aeromedically approved laser treatment modalities, without aeromedically significant visual field defect within the central 30 degrees of either eye. Second, a full binocular visual field is documented. Finally, no evidence of visual or systemic medication side effects. The degree of systemic beta-blockade resulting from ophthalmic timolol is proportionately much less than oral, with perhaps a 20-30% reduction in reflex cardiovascular responses at the plasma levels achieved with such therapy. All topical eye drop medication are aeromedically approved after an uneventful one-week ground trial. Laser surgical procedures such as argon laser trabeculoplasty (ALT), selective laser trabeculoplasty (SLT), peripheral iridotomy (PI), or iridoplasty may be performed on aviators with demonstrated uncontrolled OHT or progressive glaucoma. Waiver request for these procedures should be submitted following successful laser treatment once the treated eye/s have stabilized (usually at least one month), IOP is controlled and topical post-op steroids have been discontinued. Incisional surgery such as trabeculotomy or glaucoma shunt surgery has no waiver potential for aircrew trained or untrained.

By definition, the diagnosis of Ocular Hypertension (OHT) requires <u>absence of</u> optic nerve damage (as defined by normal 30-2 visual fields, no retinal nerve fiber layer (RNFL) or ganglion cell layer (GCL) thinning, and non-progressive optic nerve cupping). Ocular Hypertension (OHT) is disqualifying for *initial* FC I/IA, II, III, ATC, and SWA applicants provided the following conditions are met: either the intraocular pressure (IOP) is greater than 26mm Hg or the corneal thickness is less than 540um with an IOP greater than 21. Otherwise, this condition meets standards for both initial and trained aircrew.

Waiver request and Aeromedical Consultation Service (ACS) case review is not required for symmetric or asymmetric physiologic (normal variant) enlargement of the optic nerve cup.

Table 1: Waiver potential for Glaucoma (trained aircrew only)<sup>1,2</sup>

| Flying Class (FC)    | Waiver Potential | Waiver Authority | ACS Review or<br>Evaluation |
|----------------------|------------------|------------------|-----------------------------|
| II/RPA Pilot/III     | Yes              | MAJCOM           | Yes                         |
| ATC/SWA              | Yes              | MAJCOM           | Yes                         |
| GBO/OSF <sup>3</sup> | N/A              | N/A              | N/A                         |

- 1. There is no waiver potential for initial applicants with Glaucoma or Ocular Hypertension with an IOP greater than 26 mmHg or corneal thickness less than 540 um with an IOP greater than 21 mmHg.
- 2. Glaucoma for the setting of waiver criteria is defined as any history of an IOP of 30 or greater or the presence of glaucomatous optic neuropathy. Only trained aircrew will be considered for a waiver recommendation.
- 3. Only disqualifying if there is glaucoma progression NOT amenable to treatment (C6)

Table 2: Qualification Matrix for Ocular Hypertension (initial aircrew only)<sup>1</sup>

| Corneal Thickness | IOP = 21-26 mmHg | IOP > 26 mmHg |
|-------------------|------------------|---------------|
| > 540 um          | Yes              | No            |
| < 540 um          | No               | No            |

<sup>1.</sup> Ocular Hypertension (IOP greater than 21 mmHg, but less than 30 mmHg with normal OCT and visual field) in *trained* aircrew is *not* disqualifying.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

## A. Initial Waiver Request:

- 1. Aeromedical summary with a thorough review of past medical history and family history. Past ocular history should include a review of eye injuries, surgery, previous infectious or inflammatory eye disease, intraocular pressure history, previous visual field findings and presence or absence of associated risk factors including family history of glaucoma.
- 2. Complete eye examination to include:
  - a. Refraction to best visual acuity.
  - b. Humphrey visual field testing (30-2).
  - c. Applanation tonometry with diurnal measurements (at least three measurements, performed two hours apart).
  - d. Dilated funduscopic exam, and retinal nerve fiber layer analysis by optical coherence tomography (OCT) results.
  - e. OHT and glaucoma examination should also include central corneal thickness by ultrasound or with other computerized devices, such as Pentacam or anterior segment OCT (if available), and include optic disc photographs (if available).

- 3. Results of ophthalmology consultation (if required).
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

ACS review is required for all flying classes for waiver recommendation of OHT and glaucoma as part of the Ocular Hypertension/Glaucoma Management Group. A Medical Evaluation Board (MEB) is required for glaucoma if there are changes in the optic disc, visual field defects, or the condition is not amenable to treatment. An MEB is not required for ocular hypertension.

# B. Renewal Waiver Request:

- 1 Summary of any changes with a review of history and a list of quarterly measurements of intraocular pressure by applanation tonometry, unless the treating specialist specifies less frequent assessment.
- 2 A complete eye examination to include: retinal nerve fiber layer analysis by optical coherence tomography (OCT), dilated funduscopic exam with optic disc photographs, and Humphrey visual field exam (30-2) of each eye separately (if OCT abnormal).
- 3 Results of ophthalmology consultation (if required).
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Enlarged optic nerve cupping and OHT may be indicators of early glaucoma. Elevated IOP may result in difficulty with night vision secondary to the appearance of halos and flares around lights, and decreased contrast sensitivity. Left undiagnosed or inadequately treated, glaucoma can cause acquired changes in color vision, loss of central or peripheral visual fields, loss of visual acuity, and blindness. All of these visual disturbances have the potential to impair the aviator's visual performance and may present a significant safety hazard or adversely impact mission effectiveness. Glaucoma associated visual degradation occurs insidiously without subjective complaints which makes the screening program even more vital.

AIMWITS search in Jun 2019 for the previous five years revealed 444 members with an aeromedical summary with the diagnoses of glaucoma or intraocular hypertension. There 48 disqualifications. Breakdown of the cases revealed: 41 FC I/IA cases (18 disqualified), 170 FC II cases (5 disqualified), 16 RPA pilot cases (1 disqualified), 178 FC III cases (23 disqualified), 33 ATC/GBC cases (0 disqualified), 3 MOD cases (0 disqualified), and 3 SWA cases (1 disqualified).

| ICD-9 codes for optic nerve cupping, intraocular hypertension, and glaucoma |   |  |
|---|---|--|
| 743.57  | Specified anomalies of optic disc (increased cup-to-disc ratio) |  |
| 365.04  | Ocular Hypertension   |  |
| 365   | Glaucoma  |  |

| ICD-10 codes for optic nerve cupping, intraocular hypertension, and glaucoma |  |  |
|--|--|--|
| Q14.2  | Congenital Malformation of optic disc                        |  |
| H40.05   | Ocular Hypertension, right eye, left, bilateral, unspecified |  |
| 1, 2, 3, 9   |  |  |
| H40.9  | Unspecified glaucoma   |  |
| H40.10X0   | Unspecified open-angle glaucoma, stage unspecified           |  |

# **IV. Suggested Readings**

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- 2. Saeedi OJ, Ramulu P, and Friedman DS. Epidemiology of Glaucoma. Ch. 10.1 in *Yanoff: Ophthalmology*, 4<sup>th</sup> ed., Saunders, 2013.
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#### WAIVER GUIDE

Updated: Jun 2017

Supersedes Waiver Guide of Jul 2013

By: Lt Col Ric Speakman (RAM 18) and Dr Dan Van Syoc

Reviewed by Lt Col Michelle Sit, AF/SG consultant for rheumatology

# **CONDITION:** Gout (Jun 2017)

## I. Waiver Consideration.

Gout with frequent acute exacerbations in spite of therapy, or with severe bone, joint, or kidney disease is disqualifying for all Flying Classes, ATC, GBO, and SWA duties, as well as for retention. Any history of gout is disqualifying for flying classes, I, II, III, and SWA.

**Table 1: Waiver potential for gout** 

| Standard  | Gout Status               | Waiver Potential  |
|-----------|---------------------------|-------------------|
|           |                           | Waiver Authority† |
| FC I/IA   | History of Gout           | No                |
|           |                           | AETC              |
| FC II/III | History of Gout           | Yes               |
| SWA       |                           | MAJCOM            |
|           | Treated with allopurinol, | Yes               |
|           | probenecid, or NSAIDs*    | MAJCOM            |
|           | Colchicine                | No                |
|           |                           | MAJCOM            |
| ATC, GBO  | Treated with allopurinol, | Yes               |
|           | probenecid, or NSAIDs*    | MAJCOM            |
|           | Calabiaina                | No                |
|           | Colchicine                | No                |
|           |                           | MAJCOM            |

<sup>\*</sup> NSAIDs currently on approved career field specific medication list.

Review of AIMWTS data in Feb 2017 revealed a total of 710 cases related to hyperuricemia and/or gout. There were 9 FC I/IA cases, 353 FC II cases, 300 FC III, 35 ATC/GBC cases, 7 MOD cases and 6 RPA pilot cases. Of the total, there were 83 disqualifications; 5 were FC I/IA, 33 were IFC II, 36 were FC III, 8 ATC/GBC, and 1 MOD; although gout should not be waived in FC I/IA applicants, there was a single FC I case was waived for gout. The remaining FCI/IA cases listed uric acid nephrolithiasis as a diagnosis without any history of joint involvement.

<sup>†</sup>Gout with frequent exacerbations in spite of therapy, or with severe bone, joint, or kidney damage requires an MEB and AFMRA retains waiver authority. For treatment modalities not on the approved medication list, AFMSA retains waiver authority.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for gout should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. Complete history to include description of acute gouty arthritis (duration, location, response to medical treatment), risk factors (aberrant diet, alcohol intake, elevated BMI) and associated conditions (HTN, kidney stones). Negatives for risk factors and associated conditions should be included.
- C. Physical exam with special attention to joints and presence of tophi. Screening radiographs of the hands and feet as hands and feet hold wealth of information about joint health
- D. Labs: Results of joint aspiration; Serum BUN, creatinine, and uric acid. (Uric acid levels are frequently normal during attacks).
- E. If prophylaxis begun, then current medication, dose, any side effects, and uric acid level (goal
- < 6.0 mg/dL). A 24-hour urine for uric acid is required to show that the individual is not a urate over producer if started on probenecid.
- F. Consultation report from a rheumatologist or internist.
- G. MEB results if completed.

The AMS for <u>waiver renewal</u> for gout should include the following:

- A. Interim history to include any interval attacks to along with frequency, specific joint involvement, and treatment.
- B. Physical exam with special attention to joints and presence of tophi. If abnormality of joints or tophi, then x-rays of involved area.
- C. If on prophylactic treatment then annual uric acid level (goal <6.0 mg/dL) on medications and current medication, dose and side effects experienced.
- D. Consultation report from a rheumatologist or internist.

## III. Overview.

Gout is a recurrent, often monoarticular, acute arthritis resulting from the deposition of urate crystals within joint spaces and in adjacent cartilage and tendons. Fundamental to the development of gout is a substantial increase in total body uric acid stores, as reflected in the metabolic disorder hyperuricemia. It is important to realize that all patients with gout have hyperuricemia (serum uric acid level exceeding 6.8 mg/dL), but the clear majority of hyperuricemic individuals never experience a clinical event resulting from urate crystal deposition. Gout is a very common disease accounting for an estimated 7 million outpatient visits annually in the United States. Estimates of the prevalence of gout in the United States are estimated to exceed 8 million. Both the incidence and prevalence of the gout appear to be increasing in both the United States and worldwide. The estimated prevalence of gout is 3.9% in the US. The disease attacks men

disproportionately, with 73% occurring in men. Gout is predominantly an idiopathic or multifactorial disease of adult men, with a peak incidence in the fifth decade and it rarely occurs in men before adolescence or in women before menopause.<sup>1, 2</sup>

Uric acid the end-product of purine metabolism in humans. Most mammals utilize uricase, an enzyme that oxidases uric acid to allantoin. Since humans do not have this ability, the accumulation uric acid is possible by either overproduction of purine metabolites or under-excretion of urate by the kidneys. Hyperuricemia most often (90%) results from insufficient renal excretion. There are genetic causes for both causes of hyperuricemia. Hyperuricemia is a prerequisite to developing gout, but only 20% of individuals with hyperuricemia will ever develop gout. Gout can be categorized into three classic stages: asymptomatic hyperuricemia, acute intermittent gout and chronic advanced gout. Gout can also result in renal disease involving glomerular, tubular, interstitial tissues and blood vessels, and uric acid nephrolithiasis.<sup>2</sup>

The initial episode of an acute gout attack usually follows decades of asymptomatic hyperuricemia. In men, it occurs nominally between the fourth and sixth decades while it is post menopause for women. As the increased concentration of urate exceeds 6.8 mg/dL the uric acid start to form insoluble monosodium urate (MSU) crystals in a lattice formation often in joints. During the acute attack, the lattice shatters and massive numbers of MSU crystals are released in to the joint space. This acute gout is hallmarked by joint pain, swelling, warmth, and erythema. The pain reaches a crescendo within 12 hours. Joint involvement is usually monoarticular and most commonly involve the lower extremity. Gout is also self-limiting with resolution of symptoms in 5-8 days without treatment. The gouty symptoms can be thought of as an inflammatory reaction inside the joint from the MSU crystals.

Untreated gout will progress to chronic polyarticular gout or advanced gout. This stage often occurs after a decade of pain free inter-critical periods have disappeared. Intense painful flairs now occur on top of baseline joint pain. Subcutaneous tophus is characteristic of advanced gout. These tophi may develop anywhere on the body.<sup>2</sup>

The diagnosis of gout is NOT dependent on hyperuricemia. As described above, hyperuricemia is not specific to gout. Interestingly, during an acute gouty flare, urate levels may drop as much as 2.0 mg/dL limiting the utility of this test in the diagnosis of gout. The "gold standard" of gout is demonstrating MSU crystals present in the acute joint. MSU crystals appear needle-shaped and negatively birefringent with polarized light. It should be noted that only 10% of patients have synovial fluid confirmation. Most commonly is a presumptive diagnosis based on the pattern of acute joint symptoms.<sup>2</sup>

The American College of Rheumatology published diagnostic criteria for gout in 2012. If MSU are found in synovial fluid or tophus is proven to contain urate crystals, then the gold standard has been met. Additionally, six or more of the following clinical, laboratory or radiologic findings should be obtained for a provisional diagnosis:<sup>1</sup>

Asymmetric swelling with a joint on radiography Attack of monoarticular arthritis

Culture of joint fluid negative for microorganisms during attack of joint inflammation

Development of maximal inflammation within one day Hyperuricemia

Joint redness

More than one attack of acute arthritis

Nephrolithiasis occurs in 10 to 25 percent of patients with primary gout. The likelihood of stones in each patient with gout increases with serum urate concentrations and with amounts of urinary uric acid excretion. It exceeds 50 percent with a serum urate level above 13 mg/dl or with urinary uric acid excretion rates more than 1100 mg every 24-hours.<sup>2</sup>

Treatment of gout focuses on the acute attack and preventing future attacks. In the acute setting, standard therapy consists of prompt treatment of the pain and disability with nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs given in full anti-inflammatory doses are effective in approximately 90% of patients, and the complete resolution of signs and symptoms usually occurs in a few days. Indomethacin has been the traditional NSAID choice by clinicians but is not currently waiverable. All NSAIDs are equally effective as indomethacin. NSAIDS are cautioned with gastric intolerance or kidney injury. Colchicine is also used in the acute setting. This medicine was given FDA approval in 2009 but has been used for decades in the treatment of acute gouty flares. It is not currently a waiverable medicine and should be avoided with renal and hepatic insufficiency. Colchicine has some unpleasant gastrointestinal side effects. It is also contraindicated with clarithromycin. Finally, corticosteroids can be considered for patients that do not tolerate NSAIDS or colchicine. Corticosteroids may be delivered orally, intramuscularly or intra-articular with equal results.

Prevention is the next treatment modality to consider after the acute attack has subsided. Patient education should be stressed and dietary modifications considered. Weight loss reduces the risk of a gout attack. High-fructose corn syrup should be restricted along with purine-rich animal protein (organ meats, beef, lamb, pork and shellfish). Alcohol, especially beer should be limited. Onsumption of vegetables and low-fat dairy products should be encouraged.

If a patent has two more flares a year, 1 flare with chronic kidney disease (stage 2), tophi or a history of nephrolithiasis then pharmacologic urate lowering therapy (ULT) is recommended. As a rule, ULT should not be initiated during an acute gout attack, however once it has been initiated, it should be continued during an attack. First line ULTs are xanthine oxidase inhibitors: allopurinol (Zyloprim®) and febuxostat (Uloric®). Allopurinol is dosed to achieve the target serum urate level of less than 6 mg/dL. Febuxostat is a similar medication that was approved for use in 2009, but it is considerably more expensive than allopurinol. Probenecid is considered a second line treatment because of numerous drug interactions. It works by increasing the urinary excretion of uric acid and may be used in combination with the first line ULTs. When used daily, colchicine has also been shown to reduce flares.

## IV. Aeromedical Concerns.

Acute episodes of gout may cause significant physical incapacitation due to painful joints and cognitive impairment due to distraction of pain. In addition, the risk of nephrolithiasis increases modestly with the serum urate level and with the magnitude of daily urinary uric acid excretion. Chronically, gout may cause significant physical incapacitation due to erosive joint deformities, urate nephropathy, and/or obstructive uropathy (e.g. nephrolithiasis).

NSAIDs can cause gastritis acutely; chronic use can result in peptic ulcer disease and both chronic and acute renal insufficiency. Colchicine may cause diarrhea in the typical prophylactic dose and it usually causes moderate to severe intestinal cramping and vomiting if given intravenous or in high dose orally to abort acute gout. All ULT drugs can precipitate an attack of acute gouty arthritis as serum uric acid levels are lowered. Up to 5% of patients are unable to tolerate allopurinol because of adverse events including headache and gastrointestinal irritation, and less commonly, but far more serious, is the occurrence of severe hypersensitivity reactions and bone marrow suppression.

The major questions to be answered prior to requesting a waiver include: Are the gouty attacks frequent and severe? Is the patient free of renal involvement? Is the serum uric acid kept at normal levels with medication and is the patient free of untoward side effects of the medication prescribed? All of these are important considerations for an airman with gout.<sup>12</sup>

| ICD-9 codes for gout |                   |  |
|----------------------|-------------------|--|
| 274                  | Gout              |  |
| 274.0                | Gouty arthropathy |  |
| 274.1                | Gouty nephropathy |  |
| 274.82               | Tophaceous gout   |  |
| 274.9                | Gout, unspecified |  |

| ICD-10 codes fo | ICD-10 codes for gout                          |  |  |
|-----------------|--|--|--|
| M10.00          | Idiopathic gout, unspecified site              |  |  |
| M1A.9XX0        | Chronic gout, unspecified without tophus       |  |  |
|                 | (tophi)  |  |  |
| M10.30          | Gouty due to renal impairment, unspecified     |  |  |
|                 | site   |  |  |
| M1A.9XX1        | Chronic gout, unspecified, with tophus (tophi) |  |  |
| M10.9           | Gout, unspecified                              |  |  |

#### V. References.

1. Hainer BL, Matheson, E, and Wilkes RT. Diagnosis, Treatment, and Prevention of Gout. Am Fam Physician, 2014; 90(12): 831-36.

- 2. Edwards NL. Crystal Deposition Diseases. Ch. 273 in *Goldman: Cecil Med*icine, 25<sup>th</sup> ed., Philadelphia, PA: Elsevier Saunders, 2015.
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- 6. Wallace KL, Riedel AA, Joseph-Ridge N, and Wortmann R. Increasing Prevalence of Gout and Hyperuricemia Over 10 Years Among Older Adults in a Managed Care Population. J Rheumatol, 2004; 31: 1582-87.
- 7. Roddy E, Zhang W, and Doherty M. The changing epidemiology of gout. Nat Clin Pract Rheumatol, 2007; 3: 443-49.
- 8. Lioté F and Ea HK. Gout: Update on Some Pathogenic and Clinical Aspects. Rheum Dis Clin N Am, 2006; 32: 295-311.
- 9. Dessein PH, Shipton EA, Stanwix AE, et al. Beneficial effects of weight loss associated with moderate calorie/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study. Ann Rheum Dis, 2000; 59(7): 539-43.
- 10. Choi HK, Atkinson K, Karlson EW, et al. Alcohol intake and risk of incident gout in men: a prospective study. Lancet, 2004; 363(9417): 1277-81.
- 11. Terkeltaub RA. Gout. N Engl J Med, 2003; 349: 1647-55.
- 12. Rayman RB. Internal Medicine, Ch. 6 in *Rayman's Clinical Aviation Medicine*, 5th ed., New York; Connolly Graduate Medical Publishing, LTD, 2013, pp. 148-49.

# Guillain-Barré Syndrome (Acute Inflammatory Demyelinating Polyradiculoneuropathy) (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

Updated Table 1 and References

#### I. Waiver Consideration

Guillain-Barré Syndrome (GBS) is disqualifying for all flying classes and for GBO and ATC personnel. Per Medical Standards Directory (MSD) L26: "Polyneuritis, whatever the etiology, unless: Limited to a single episode, the acute state subsided at least 1 year before examination, there are no residual effects which could be expected to interfere with normal function in any practical manner." The one-year observation period is specified to allow for maximal functional recovery and because most GBS recurrences or transformation to chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) will occur within this time frame. For flying personnel with GBS, a waiver recommendation is very likely if there is full recovery. An ACS review/evaluation is required to determine eligibility for a return to flying status if residual deficits remain after recovery, but are minor and not felt to interfere with aircrew duties. GBS is not disqualifying for SWA and OSP duties per the MSD.

Table 1: Waiver potential for Guillain-Barré Syndrome

| Flying Class (FC) | Waiver<br>Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|---------------------|------------------|--------------------------|
| FC I/IA           | Yes <sup>1</sup>    | AETC             | Yes                      |
| FC II/III         | Yes <sup>2</sup>    | MAJCOM           | Yes                      |
| ATC/GBO           | Yes <sup>2</sup>    | MAJCOM           | Yes                      |

<sup>1.</sup> IFC I/IA waiver generally not recommended for GBS patients with residual deficits.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- 2. Reports of laboratory studies, lumbar puncture, electrodiagnostic studies, imaging studies, and copies of images from any CT/MRI studies. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Neurology consultation reports, including follow-up notes with examination findings after disease resolution.

<sup>2.</sup> Trained aviators with GBS and residual deficits are considered for waiver on a case-by-case basis.

- 4. Pulmonary function testing after disease resolution.
- 5. If vision was involved, Optometry or Ophthalmology consultation, to include all tests listed in the MSD (stereopsis, ocular motility and alignment testing).
- 6. If obtained, Physical/Occupational Therapy/Rehabilitation Medicine consultation reports.
- 7. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 8. Current physical and neurologic examination findings.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- Interval history, with particular emphasis on neurologic examination findings and specific testing as annotated in the initial waiver section.
- Copies of any interim specialty notes, interim diagnostic testing, and images from any interim radiographic studies. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical and neurologic examination findings.
- 4. Comments regarding any current activity limitations.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual symptoms, signs, and medications used for treatment on operational safety and mission effectiveness, and future risk of symptom recurrence. Within six to twelve months about 85% of GBS patients have fully recovered, with maximal recovery of residual deficits usually seen within 18 months after symptom onset. Persistent minor weakness, areflexia, and paresthesias may remain, and approximately 7% to 15% of patients have permanent neurological sequelae (e.g. foot drop, intrinsic hand muscle wasting, sensory ataxia, painful dysesthesia), which could be aeromedically-significant. The relapse rate for GBS is uncommon and if this occurs, raises the possibility of the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) or other conditions. Most GBS recurrences or transformation to CIDP will occur within 6-12 months of the initial presentation.

AIMWITS search in Jun 2018 revealed a total of 15 cases of GBS. There were 8 FC II cases, 1 RPA pilot case, 5 FC III cases, and 1 MOD case. There were 3 disqualified cases; 1 FC II, 1 FC III, and 1 MOD individual who was disqualified for GBS and concomitant myasthenia gravis.

| ICD-9 codes for Guillain-Barré Syndrome |   |
|---|---|
| 357.0                                   | Acute infective polyneuritis                          |
| 357.4                                   | Polyneuropathy in other diseases classified elsewhere |
| 357.8                                   | Other inflammatory and toxic neuropathies             |

| ICD-10 codes for Guillain-Barré Syndrome |   |
|--|---|
| G61.0                                    | Acute infective polyneuritis                    |
| G63                                      | Polyneuropathy in diseases classified elsewhere |
| G61.89                                   | Other inflammatory polyneuropathies             |

# **IV. Suggested Readings**

- 1. Donofrio PD. Guillain-Barré Syndrome. Continuum (Minneap Minn) 2017; 23(5):1295-1309.
- 2. Allen JA. Chronic demyelinating polyneuropathies. Continuum (Minneap Minn) 2017; 23(5):1310-1331.
- 3. Vriesendorp F. Guillain-Barré Syndrome in adults: clinical features and diagnosis. UpToDate Dec 4, 2018.
- 4. Vriesendorp F. Guillain-Barré Syndrome in adults: treatment and prognosis. UpToDate May 21, 2019.
- 5. Diseases of the peripheral nerves. Principles of Neurology, 10<sup>th</sup> Edition (Ropper AH, Samuels MA, Klein JP Eds), McGraw-Hill 2014: 1322-1330.
- 6. Dimachkie MM, Barohn RJ. Guillain-Barre´ Syndrome and Variants. Neurol Clin N Am 2013; 31(2):491-510.
- 7. Walling AD, Dickson G. Guillain-Barré Syndrome. Am Fam Physician 2013; 87(3):191-98.

## Headache (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated Waiver Consideration, Table 1, Aeromedical Concerns and References

#### I. Waiver Consideration

All headaches, except for the occasional tension headaches, are disqualifying for all flying classes in the US Air Force according to the Air Force Medical Standards Directory. A single severe/incapacitating headache is also disqualifying, emphasizing the need to exclude serious underlying causes before returning to operational duties. A headache will be considered disqualifying if any of the following characteristics are present:

- A. Impairment in social, vocational or academic activities caused by the headache and/or its associated symptoms.
- B. Medication other than non-prescription type required for abortive control of the headache.
- C. Prescription medication is required for headache prophylaxis.
- D. There is associated neurologic dysfunction or deficit including aura, with or without (i.e., acephalgic migraine) associated headache.

The waiver authority may consider a waiver if these criteria are fulfilled:

- A. Three or fewer disqualifying headaches per year, and,
- B. There is no associated neurologic dysfunction, deficit or aura, and,
- C. There exists negligible or mild functional impairment (i.e., did not cause significant social or occupational impairment), nausea, photophobia, or phonophobia, **and**,
- D. No prescription prophylactic or abortive medication is required.

All other cases may have ACS review at discretion of the waiver authority. Note that an ACS review does not imply a return to operations waiver recommendation. None of the current FDA-approved prophylactic pharmacologic therapies are formally aeromedically-approved for use in USAF aviators, although rarely some agents these have been recommended for waiver in exceptional cases (see Aeromedical Concerns section). Several triptan medications are currently approved for use in USAF aviators, but not for IFC I/IA or unrestricted FC II. If triptan agents are used, there should be a 24-hour DNIA/C/F period following the last triptan dose taken, to allow for medication clearance and symptom resolution. It is important to note that the underlying headache diagnosis must first meet waiver suitability before any medication use is then considered.

**Table 1: Waiver potential for headaches** 

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation          |
|-------------------|------------------|------------------|-----------------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | At discretion of waiver authority |
| FC II//III/SWA    | Yes <sup>2</sup> | MAJCOM           | At discretion of waiver authority |
| ATC/GBO           | Yes <sup>2</sup> | MAJCOM           | At discretion of waiver authority |

<sup>1.</sup> IFC I/IA candidates with secondarily provoked headaches, or with primary headaches and a long headache-free interval are considered for waiver on an individual basis.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations. While there is no longer any required minimum observation period before waiver application, there should be a reasonable observation period to ensure continued headache control and clinical stability.

# A. Initial Waiver Request:

- 1. Detailed history of the headaches; age at onset; presence or absence of aura and prodrome; frequency, intensity and duration of attacks; number of headaches per month; date of last headache attack; time and mode of onset; quality, site, and radiation of pain; associated symptoms and abnormalities; family history of headaches; precipitating and relieving factors; effect of activity on pain; relationship with food/alcohol; response to any previous therapies; any recent change in vision; any recent trauma; recent changes in weight, exercise, sleep, or diet; state of general health; change in work or lifestyle; change in birth control methods (women): effects of menstrual cycle and exogenous hormones (women); and any association with environmental factors.
- 2. Current physical and neurologic examinations.
- 3. Noncontrast brain MRI study unless contraindicated.
- 4. Imaging study reports and copies of images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 5. Specialty consultation reports and results of any diagnostic studies.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1 Interval history and timeline of disease include details listed in II.A.1. as applicable.
- 2 Copies of any interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical and neurologic examination findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

<sup>2.</sup> History of migraine or other headache types are considered for waiver on an individual basis. Waiver recommendation for cluster headache is unlikely except in cases of prolonged remission.

## **III. Aeromedical Concerns**

Aeromedical concerns with headache relate to the impact of any neurologic or cognitive deficits and any medication-related effects on operational safety and mission effectiveness, and future risk of headache occurrence, with potential for incapacitation or distraction. The primary concerns in aeromedical disposition of a given aviator are the degree of incapacitation a headache is likely to cause and the future likelihood of recurrence, with the actual headache diagnosis a secondary consideration. Associated features such as visual disturbance, vomiting, or vertigo could by themselves lead to incapacitation during flight. Concern is greatest for those flying single-seat aircraft or in aircraft where complete crew participation and coordination is essential for mission completion, but significant concerns exist for any aircrew member in any type of aircraft. Unfortunately, the future recurrence risk for most headache disorders is imprecisely predictable. Past historical patterns are useful only as an estimate of future activity. Sufficient observation time should be obtained to reasonably ensure stability; this time will vary by the individual and headache type. Appropriate headache therapy is dependent on a correct and complete diagnosis. Non-pharmacologic strategies such as lifestyle modification and behavioral techniques can be useful management adjuncts. Selected patients may benefit from measures such as dietary supplements, osteopathic manipulation, trigger point injections or acupuncture. Many FDA-approved headache medications are not aeromedically-approved for use or are potentially waiverable. Antihypertensive medications have occasionally been recommended for non-high performance aircraft waiver. Antidepressant and anticonvulsant medications are currently not recommended for waiver for pilots of manned or unmanned aircraft. Treatment with chemodenervation (usually with botulinum toxin) or external stimulator devices will not be recommended for aeromedical waiver due to the requirement for very frequent headaches as an indication for chemodenervation, and operational concerns on use of external stimulators. Calcitonin gene-related polypeptide (CGRP) antagonists and modulators are relatively newly approved for use in the USA, and currently are not recommended for aeromedical waiver. The Flight Surgeon needs to be cognizant of secondary disorders or provocative factors, and should also look for the possibility of medication overuse. Obtaining a social history to look for potential effects of tobacco use, ethanol use and caffeine intake is important. Maintaining a headache diary/calendar is useful to identify possible triggering factors and assess treatment response. Characteristics such as sudden onset of severe symptoms, new headache with history suspicious for meningitis or concerning laboratory findings, worsened degree of a chronic headache, abnormal examination findings, or unclear diagnosis would warrant further investigation.

AIMWTS review in Jan 2019 revealed 2301 members with a waiver submissions including the diagnosis of headache. Of these, there were 1211 disqualifications. Breakdown of the cases was as follows: 180 FC I/IA cases (95 disqualified), 439 FC II cases (161 disqualified), 60 RPA pilot cases (13 disqualified), 1000 FC III cases (580 disqualified), 403 ATC/GBC cases (278 disqualified), and 219 MOD cases (89 disqualified). The vast majority of DQ cases were primarily for the headache diagnosis.

| Selected ICD-9 codes for Headache |                                |  |
|-----------------------------------|--------------------------------|--|
| 784.0                             | Headache (generic code)        |  |
| 346.0                             | Classical migraine             |  |
| 346.1                             | Common migraine                |  |
| 346.2                             | Variants of migraine           |  |
| 346.8                             | Other forms of migraine        |  |
| 346.9                             | Migraine, unspecified          |  |
| 339.11                            | Episodic tension-type headache |  |
| 339.01                            | Episodic cluster headache      |  |

| Selected ICD-10 | Selected ICD-10 codes for Headache              |  |  |
|-----------------|---|--|--|
| R51             | Headache (generic code)                         |  |  |
| G43.109         | Migraine with aura, not intractable, without    |  |  |
|                 | status migrainosus                              |  |  |
| G43.009         | Migraine without aura, not intractable,         |  |  |
|                 | without status migrainosus                      |  |  |
| G43.809         | Other migraine, not intractable, without status |  |  |
|                 | migrainosus                                     |  |  |
| G44             | Vascular headache, not elsewhere classified     |  |  |
| G44.219         | Episodic tension-type headache                  |  |  |
| G44.019         | Episodic cluster headache not intractable       |  |  |

# **IV. Suggested Readings**

- 1. Smith JH. Acute treatment of migraine in adults. UpToDate, Feb 13, 2020.
- 2. Smith JH. Preventive treatment of migraine in adults. UpToDate, Feb 14, 2020.
- 3. Wootton RJ, Wippold II FJ. Evaluation of headache in adults. UpToDate, Nov 12, 2019.
- 4. Cutrer FM et al. Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. UpToDate, Nov 15, 2019.
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- 7. Burish M. Cluster headache and other trigeminal autonomic cephalalgias. Continuum (Minneap Minn) 2018; 24(4):1137-1156.
- 8. Tepper SJ. Cranial neuralgias. Continuum (Minneap Minn) 2018; 24(4):1157-1178.
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- 10. Taylor FR. Tension-type headache in adults: preventive treatment. UpToDate, Aug 20, 2018.
- 11. Tepper SJ. Nutraceutical and other modalities for the treatment of headache. Continuum (Minneap Minn) 2015; 21(4):1018-1031.

# Hearing Loss/Asymmetric Hearing Loss/Use of Hearing Aid(s) (Apr 2019)

Reviewed: Lt Col Marshall Hayes (RAM 20), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), Lt Col Brandon Tourtillott (AF/SG Audiology consultant), Lt Col Wesley Abadie (AF/SG Otolaryngology consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Format

#### I. Waiver Consideration

Hearing loss that precludes safe, effective performance of duty despite use of hearing aid(s) (i.e. H-4) is disqualifying for all flying and special duty personnel, as well as retention. Use of a hearing aid is disqualifying for FC I/IA, II, III, ATC, and SWA. Initial applicants for FC I/IA, II, III, ATC, SWA and RPA must be H1 for selection; initial applicants for GBO personnel (with exception of RPA pilot) require H2. FC II, FC III, SWA, and RPA trained assets with H2 require evaluation for conductive or retrocochlear pathology (includes audiology evaluation and potential ENT evaluation). Restriction from flying is not required during this work-up. No waiver is required for trained personnel unless indicated by audiology/ENT findings. Trained aviators and special duty personnel (all classes) with H-3 profiles or asymmetric hearing loss are disqualified and require aeromedical waiver.

The following table outlines the definition for H-1, H-2, H-3 and H-4 hearing profiles. The hearing profile is based on an unaided audiogram (no hearing aids) and removal from hazardous noise for at least 14 hours.

Table 1: Hearing profile standards and asymmetry definition.

|                            | 500 Hz  | 1000 Hz       | 2000 Hz       | 3000 Hz      | 4000 Hz      | 6000 Hz  |
|----------------------------|---|---------------|---------------|--------------|--------------|----------|
| H-1 Profile                |   |               |               |              |              |          |
| If no single value exceeds |   |               |               |              |              |          |
| (dB):                      | 25  | 25            | 25            | 35           | 45           | 45       |
| H-2 Profile                |   |               |               |              |              |          |
| If no single value exceeds |   |               |               |              |              |          |
| (dB):                      | 35  | 35            | 35            | 45           | 55           |          |
| H-3 Profile                | Any hearing loss exceeding at least one value for H-2 profile,          |               |               |              |              |          |
|                            | but does n  | ot qualify f  | or H4.        |              |              |          |
|                            | Hearing lo  | oss sufficier | nt to preclud | de safe and  | effective    |          |
| H-4 Profile                |   |               |               |              | pure tone he | earing   |
|                            | loss, and despite use of hearing aids. <sup>1</sup>                     |               |               |              |              |          |
|                            | Written va  | alidation of  | ability to sa | afely perfor | m all assign | ned      |
|                            | aircrew duties in flying environment signed by flying SQ/CC or          |               |               |              |              |          |
| *Hearing Proficiency       | Operations Officer, <i>supplemented by</i> the flight surgeon's written |               |               |              |              |          |
| Validation                 | memo for  | record stati  | ing that Spe  | ech Recogn   | nition Leve  | ls (from |
|                            | the audiol  | ogy report)   | are adequa    | te to perfor | m flying du  | ities    |
|                            | (>70%).   |               |               |              |              |          |
| Asymmothy                  | ≥25 dB difference comparing left and right ear, at any two              |               |               |              |              |          |
| Asymmetry                  | consecutive frequencies. <sup>1</sup>                                   |               |               |              |              |          |

<sup>1.</sup> Asymmetry at 3000 Hz is considered by recent studies to be an important predictor of retrocochlear pathology.

Waivers are valid for no greater than three years (indefinites will not be granted) or until a shift of 10 dB or greater on the average of 2,000, 3,000 and 4,000 Hz in either ear from the previous waiver's audiogram, whichever occurs first. If the cause of the hearing loss is acoustic neuroma, cholesteatoma, eustachian tube dysfunction, otosclerosis, or a peripheral vertiginous disorder, refer to the Waiver Guides for those conditions as well before preparation of the aeromedical summary.

Table 2: Degree of hearing loss and waiver potential.

| <b>Flying Class</b>      | Hearing Loss                      | Waiver Potential   | ACS Review/             |
|--------------------------|-----------------------------------|--|-------------------------|
|                          |                                   | Waiver Authority   | Evaluation <sup>7</sup> |
| I/IA                     | H-1 with asymmetry                | Yes<br>AETC  | No                      |
|                          | H-2 with or without asymmetry     | Maybe <sup>1</sup><br>AETC   | No                      |
|                          | H-3/H-4 with or without asymmetry | No<br>AETC   |                         |
|                          |                                   | No   |                         |
|                          | Hearing aids                      | AETC   |                         |
| II/III<br>ATC/GBO<br>SWA | H-2                               | Initial/untrained – Maybe <sup>2</sup> Trained – N/A <sup>3</sup> MAJCOM | As Above                |
|                          | Н-3                               | Initial/untrained – No<br>Trained – Maybe <sup>4</sup><br>MAJCOM         | As Above                |
|                          | H-4                               | No<br>MAJCOM   |                         |
|                          | Asymmetry                         | Initial/untrained – Maybe <sup>5</sup><br>Trained – Maybe<br>MAJCOM      | As Above                |
|                          | Hearing aids                      | Initial/untrained – No<br>Trained – Maybe <sup>6</sup><br>MAJCOM         | As Above                |

- 1. Waiver for FC I/IA may be considered if H-2 due to one frequency in one ear.
- 2. Waiver for initial/untrained FC II and III may be considered if H-2 due to one frequency in one ear. H-2 is qualifying for GBO applicants (with exception of RPA pilot).
- 3. For trained FC II, FC III, RPA pilots and ATC, no waiver required (need not be grounded) but must have full audiology work-up.
- 4. If individual inactive flyer, then hearing proficiency validation delayed; FC IIC or modified FC III waiver granted by MAJCOM (must have hearing proficiency validation [inflight test or letter from SQ/CC or DO] before flying).
- 5. Waiver for initial/untrained FC II and III with H-1 likely; waiver for initial/untrained FC II and III with H-2 may be considered if H-2 due to one frequency in one ear; no waiver for initial/untrained FC II and III with H-3.
- 6. If H-3 and hearing aids not worn while flying, must pass hearing proficiency validation without hearing aids.
- 7. Review by ACS is not routinely required, but can be requested on a case-by-case basis. Note: NO <u>indefinite</u> waivers will be granted for asymmetric hearing loss or H-3; maximum length of waiver is 3 years.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. <u>Initial Waiver Request:</u>

- 1. Summary of presentation, course, and treatment. Include history related to hearing loss (including noise exposure history). If hearing aids are used, include if worn while flying and address the ability to wear hearing protection.
- 2. Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated), including baseline and latest audiograms.
- 3. Any consultation reports, including follow-up notes with examination findings after disease resolution. Include documentation of complete (and current within 12 months of waiver submission) audiology evaluation. Consider otolaryngology evaluation if there is any concern for conductive or retrocochlear disease.
- 4. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 5. Validation of hearing proficiency for H-3 waivers (initial waivers and waiver renewals with a shift of 10 dB or greater on the average for 2,000, 3,000 and 4,000 Hz from the previous waiver's audiogram).
  - a. In-flight hearing test or
  - b. Written validation of ability to safely perform all assigned aircrew duties in flying environment signed by flying SQ/CC or Operations Officer, supplemented by the flight surgeon's written MFR stating that Speech Discrimination Levels (from the audiology report) are adequate to perform flying duties (≥70%).
- 6. If the local base is not able to provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

1 Same as for the initial waiver request above.

#### III. Aeromedical Concerns

It is essential that aviators have hearing adequate to recognize and understand verbal communications and warning tones. This includes adequate binaural hearing in aircraft with warning tones presented specifically to the left or right sides. Significant tinnitus associated with hearing loss may interfere with communications as well as sleep. Hearing loss can be an early symptom of other medical problems, for example, an acoustic neuroma (see Vestibular Schwannoma waiver guide) which could directly affect vestibular function and flight safety. Lastly, aviators with noise induced hearing loss will likely experience some degree of worsening hearing loss secondary to continued noise exposure.

If the design of the hearing aid allows the proper fit of hearing protection devices, and they are programmed appropriately to minimize feedback, hearing aids may be worn

during flight. Hearing aids are not a substitute for hearing protection. Lack of proper hearing protection in hazardous noise places an individual at risk for increased hearing loss. If double hearing protection is required, hearing aids are not allowed. Cochlear implants or implantable amplification devices are not allowed in any hazardous noise environment and thus not allowed in aviators. Hearing aid battery life varies, with the shortest being about 4 days; changing a battery can be disruptive to aircrew duties, thus batteries should be changed prior to flying if hearing aids are worn while performing aircrew duties.

Individuals with otosclerosis or other causes of conductive hearing loss may actually hear better in noise/flight. This is due to a phenomenon called the Paracusis of Willis; the otosclerosis filters out the background noise and allows the individual to hear communications better. In this unique situation, hearing aids may be used on the ground but not recommended or needed in flight.

Review of AIMWTS through Apr 2019 revealed 27 cases of hearing aid usage; 11 FC II cases (1 disqualified), 1 RPA pilot case, 7 FC III cases, and 8 ATC/GBC cases.

Review of AIMWTS from Jan 2014 through Apr 2019 revealed 1,058 waivers for some degree of hearing loss. There were 34 FC I/IA cases (8 disqualified), 489 FC II cases (12 disqualified), 23 RPA pilot cases (4 disqualified), 408 FC III cases (49 disqualified), 89 ATC/GBC cases (11 disqualified), and 15 MOD cases (3 disqualified).

| ICD-9 Codes for Hearing Loss and Hearing Aids |   |  |
|---|---|--|
| 389.0   | Conductive hearing loss                         |  |
| 389.1   | Sensorineural hearing loss                      |  |
| 389.16  | Sensorineural hearing loss, asymmetrical        |  |
| 389.2   | Mixed conductive and sensorineural hearing loss |  |
| V53.2   | Hearing aid                                     |  |

| ICD-10 Codes for Hearing Loss and Hearing Aids |   |  |
|--|---|--|
| H90  | Conductive hearing loss, bilateral, unspecified             |  |
| 0, 2   |   |  |
| H90  | Sensorineural hearing loss, bilateral, unspecified          |  |
| 3, 5   |   |  |
| H90  | Mixed conductive and sensorineural hearing loss, bilateral, |  |
| 6, 8   | unspecified   |  |
| Z97.4  | Presence of external hearing-aid                            |  |

# **IV. Suggested Readings**

- 1. AFI 48-127, Occupational Noise and Hearing Conservation Program, 26 February 2016.
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## **WAIVER GUIDE**

Updated: Jul 2014

Supersedes Waiver Guide of Mar 2011

By: Dr Dan Van Syoc

Reviewed by Lt Col Timothy Phillips, AF/SG consultant for Urology and Lt Col Eric

Barnes, AF/SG consultant for Nephrology

## **CONDITION:**

Hematuria (Jul 2014)

## I. Waiver Consideration.

Hematuria by itself is not disqualifying for flying classes I/IA, II, III and SWA duties. It is also not disqualifying for retention purposes, for ATC and GBO duties. While hematuria itself is not disqualifying, the underlying cause (such as calculi) may be disqualifying or require waiver. No waiver required if fully evaluated and final diagnosis is benign or idiopathic with appropriate follow-up.

**Table 1: Waiver potential for hematuria** 

| Flying Class (FC)     | Condition              | Waiver Potential |
|-----------------------|------------------------|------------------|
|                       |                        | Waiver Authority |
| I/IA                  | "Benign" or idiopathic | N/A              |
|                       | Calculi†               | Maybe<br>AETC    |
|                       | Other causes*          | Maybe<br>AETC    |
| II/III<br>ATC/GBO/SWA | "Benign" or idiopathic | N/A              |
|                       |                        | Maybe            |
|                       | Calculi†               | MAJCOM           |
|                       |                        | Maybe            |
|                       | Other causes*&         | AETC**           |

<sup>†</sup>See Renal Stones waiver guide for details

AIMWITS search in Jul 2014 revealed a total of 514 members with an AMS for the diagnosis of hematuria. Breakdown of the cases revealed: 47 FC I/IA cases (11 disqualified), 198 FC II cases (8 disqualified), 248 FC III cases (30 disqualified), 13 ATC/GBC cases (1 disqualified), and 8 MOD cases (1 disqualified). Almost all of the disqualifications were due to other medical problems, or if it was due to hematuria, there

<sup>\*</sup>IgA nephropathy, glomerulonephritis, cancer, etc.

<sup>&</sup>amp; Untrained personnel will need to be evaluated similarly as for FC I/IA

<sup>\*\*</sup> AFMRA is waiver authority if retention standards are applicable

were other renal issues as well. In the ATC/GBC and MOD cases, the underlying reason for the waiver submission was not hematuria. For future waiver guide updates, the total number of cases will be much less as only a small percentage of cases with hematuria will require a waiver to be submitted.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

For flying classes I/IA, II, IIU, and III, a waiver for the finding of microscopic hematuria only (if proteinuria also seen in urinalysis then initiate steps J through L listed below concurrently) is not necessary. An initial work-up of hematuria, though, should include the following:

- A. Thorough history to identify possible sources for hematuria, upper versus lower tract, and identification of risk factors for malignancy.
- B. Examination of external urethra and prostate (male) or pelvis (female).
- C. Urinalysis and urine culture.
- D. Serum BUN and creatinine.
- E. Repeat urinalysis 48 hours after cessation of menstruation, analgesic medications, vigorous exercise, or sexual activity. Repeat urinalysis 6 weeks after treatment of a urinary tract infection.

In individuals where the above information supports a "benign" cause (menstruation, analgesic medications, vigorous exercise, sexual activity, and/or the resolution of a urinary tract infection) and the repeat urinalysis is normal, no further workup is required.

- If A F above does not point to a "benign" cause of the hematuria (menstruation, analgesic medications, vigorous exercise, sexual activity, and/or the resolution of a urinary tract infection), the aeromedical summary is required to contain the following additional elements:
- G. Radiographic evaluation of upper tract CT, IVP and/or ultrasound (helical CT with and without contrast is now upper tract imaging procedure of choice, if available).
- H. Urology consult (to include cystoscopy if indicated) should follow upper tract imaging, particularly if risk factors for malignancy are identified.
- I. If no urological etiology is found, consultation with a nephrologist for possible renal biopsy should be obtained.

If proteinuria, dysmorphic red blood cells, red cell casts, or elevated serum creatinine level is present, the following additional work-up is required:

- J. Complete blood count (CBC).
- K. 24-hour urine for creatinine and protein, if urinallysis positive for protein.
- L. Nephrology consultation to include consideration of a renal biopsy.

If a cause for the hematuria is determined such as calculi, IgA nephropathy, glomerulonephritis or cancer, then waivers will be also be needed for those diagnoses. Current waiver guides exist for renal stones, IgA nephropathy, and bladder cancer which need to be adhered to if that diagnosis is applicable.

#### III. Overview.

Gross hematuria is relatively common - one out of every 1000 visits to the emergency room is prompted by a patient's discovery of gross hematuria. Asymptomatic microscopic hematuria (AMH) is even more common, with a prevalence of 1.2% to 5.2% in young adult males, and as high as 16% to 21% in community population-based studies. Discovering the underlying process, if any, causing the hematuria is the key to a proper aeromedical disposition. Some emergency department estimates are that the underlying cause of hematuria is elusive in as many as 61% of cases. The risk factors for significant underlying disease include: cigarette smoking, occupational exposure (benzene, aromatic amines), history of gross hematuria, age greater than 35 years, history of urologic disorder or disease, urinary tract infection, analgesic abuse, irritative voiding symptoms, pelvic radiation, and cyclophosphamide use. Screening for hematuria in patients with no symptoms suggestive of urinary tract disease is not recommended by any medical body.

Hematuria may be transient and common causes of such cases are vigorous physical exercise, sexual intercourse, trauma, digital rectal examination, or menstrual contamination. If a transient etiology is suspected, the clinician should order a follow-up urinalysis 48 hours after the positive test and a negative result will probably confirm the diagnosis of transient hematuria.<sup>7,8</sup> The most common <u>non-transient</u> causes of hematuria in adults include urinary tract infections, stone disease, benign prostatic enlargement and a urologic malignancy.<sup>9</sup>

A positive dipstick for blood in urine indicates hematuria, hemoglobinuria or myoglobinuria. Hematuria can be distinguished from hemoglobinuria and myoglobinuria by microscopic examination of the centrifuged urine; the presence of a large number of erythrocytes establishes the diagnosis of hematuria. If erythrocytes are absent, examination of the serum will distinguish hemoglobinuria and myoglobinuria. In hemoglobinuria, the supernatant will be pink and in myoglobinuria, the serum remains clear. Dipsticks for heme detect 1 to 2 RBCs per high powered field (HPF) which is equivalent to the sensitivity of urine sediment examination, but will result in more false positive tests. The American Urologic Association has stated that the most accepted upper limit of normal for urinary RBCs, based on an exam of the urinary sediment, is <3 per HPF. Asymptomatic microscopic hematuria is defined as 3 or greater RBCs per HPF on a single properly collected urinary specimen in the absence of obvious benign cause. <sup>10</sup>

Hematuria of nephrologic origin is frequently associated with casts in the urine and almost always associated with significant proteinuria. Protein in the urine greater than 200mg/24 hours is of nephrologic origin; significant hematuria from a urologic origin will not elevate protein that high. Erythrocytes arising from glomerular disease are typically dysmorphic and show a wide range of morphologic alteration. Conversely, erythrocytes

arising from tubulointerstitial renal disease and of urologic origin have a uniformly round shape. 11

Hematuria may be essentially a normal variant, or it may be a sign of underlying disease, which may possibly even be life-threatening. For the purposes of evaluation and diagnosis, hematuria is divided into two general categories: glomerular and non-glomerular.

Glomerular hematuria (loss of blood into urinary tract from glomeruli) is frequently associated with proteinuria, protein or RBC casts, and dysmorphic RBCs on phase-contrast microscopy. The differential diagnosis of hematuria with proteinuria or casts is extensive, and includes nephron damage and many forms of glomerulonephritis. The most common glomerular sources have been found to be IgA nephropathy (Berger's disease) and thin glomerular basement membrane disease.<sup>7</sup>

Non-glomerular hematuria is blood that enters the urinary tract distal to glomeruli, so that RBCs have normal morphology on phase-contrast microscopy. Proteinuria and casts are not normally associated with non-glomerular hematuria. The most common non-glomerular sources are stones, infection and malignancy. In six major studies of microscopic hematuria, between 1% and 12.5% had a neoplastic etiology and between 3.5% and 16.5% had calculi as the etiology. In one study of 161 aviators with asymptomatic microscopic hematuria, no evident pathology developed over a mean follow-up period of 7.6 years. <sup>11, 12</sup>

The differential diagnosis of asymptomatic hematuria without proteinuria or casts (e.g. non-glomerular hematuria) includes neoplasm, calculi, infection, trauma (including exercise), analgesic use/abuse and sickle cell nephropathies. Bleeding into the urinary tract from a source between the urethra and the renal pelvis will result in no protein, cells or casts. Hematuria at the beginning or end of the stream usually indicates a urethral or prostatic source.

Once infectious and glomerular etiologies of hematuria have been ruled out, other etiologies will need to be considered. The consensus among urologists is that patients presenting with hematuria less than 35 years of age and no risk factors should at a minimum have upper tract imaging with CT urography or other modalities as directed below. Cystoscopy need only be performed in this group of patients at the discretion of a urologist. For the remainder of cases (≥35 years old or risk factors), a complete urologic evaluation to include imaging and cystoscopy is indicated.¹¹¹ Cystoscopy is utilized to directly visualize the lining of the bladder to detect evidence of bladder cancer. The goal of imaging is to detect neoplasms, urinary tract calculi, renal cystic disease, and obstructive lesions that could be responsible for the hematuria.¹¹² Most clinicians consider multidetector CT urography to be the preferred initial imaging modality in most patients presenting with unexplained hematuria. Other modalities used include intravenous pyelography (IVP), ultrasonography, MR urography, retrograde pyelography with plain films. <sup>6,10</sup>

A negative evaluation for a patient with asymptomatic microscopic hematuria is good news for the patient. But each of these folks deserves some sort of follow-up as reports have shown that 1% to 3% of these patients may progress to a urologic malignancy within three years and another small proportion can also develop renal insufficiency. <sup>13</sup>

The American Urological Association (AUA) Guideline: Diagnosis, Evaluation and Follow-up of Asymptomatic Microhematuria (AMH) in Adults (Table 1 and Figure 1 below):

Table 2. Common Risk Factors for Urinary Tract Malignancy in Patients with Microhematuria  $^{10}$ 

| Table 1:                                   |
|--|
| Common Risk Factors for Urinary Tract      |
| Malignancy in Patients with Microhematuria |

Male gender

Age (> 35 years)

Past or current smoking

Occupational or other exposure to chemicals or dyes (benzenes or aromatic amines)

Analgesic abuse

History of gross hematuria

History of urologic disorder or disease

History of irritative voiding symptoms

History of pelvic irradiation

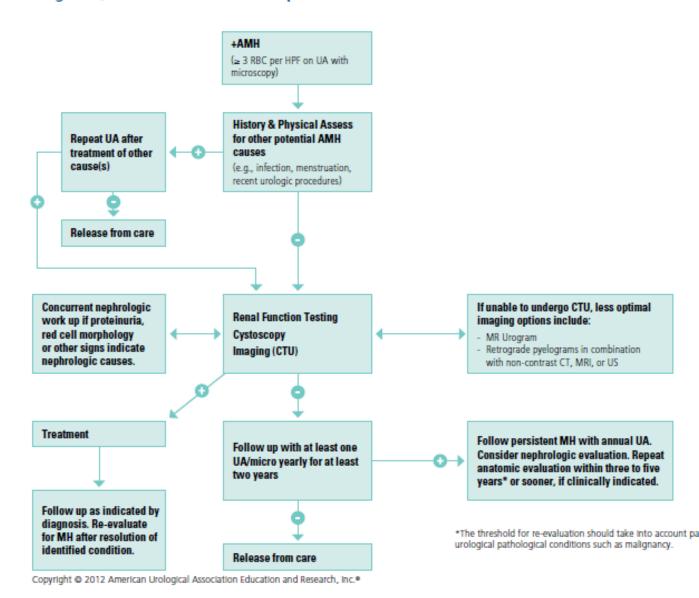
History of chronic urinary tract infection

History of exposure to known carcinogenic agents or chemotherapy such as alkylating agents

History of chronic indwelling foreign body

# FIGURE 1. Algorithm for Evaluation and Follow-up of Asymptomatic Microhematuria

## Diagnosis, Evaluation and Follow-up of AMH



#### IV. Aeromedical Concerns.

Persistent or recurrent hematuria is not disqualifying, unless an underlying etiology is identified. Because hematuria can be a sign of significant underlying disease, it must be evaluated fully. Calculi can cause extreme pain, lead to urinary tract infection and obstruction and/or result in sudden incapacitation while in flight. Urinary neoplasms are often slow growing but must be diagnosed and treated early to optimize survival and function. Glomerular disease must be evaluated and renal function assessed to determine

proper treatment and to address worldwide deployability (e.g. renal reserve, ability to tolerate dehydration, etc.).

| ICD-9 code for | · hematuria |
|----------------|-------------|
| 599.7          | Hematuria   |

| ICD-10 codes for hematuria |                             |
|----------------------------|-----------------------------|
| R31.9                      | Hematuria, unspecified      |
| R31.2                      | Other microscopic hematuria |

#### V. References.

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#### WAIVER GUIDE

Updated: Oct 2014

Supersedes Waiver Guide of Mar 2010

By: Capt Karen A Rupp (RAM XV) and Dr Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology and Col

Pat Storms, RAM and gastroenterologist

## **CONDITION:**

Hemochromatosis (Oct 2014)

#### I. Waiver Consideration.

Hemochromatosis (HH) is disqualifying for all flying classes, as well as for ATC/GBO and SWA duties. It is not waiverable for initial flying training. It is potentially waiverable if the member has no aeromedically significant complications from the HH and is on maintenance phlebotomy. Maintenance phlebotomy to maintain control of iron stores will require a 72-hour DNIF after each phlebotomy for FC II, FC III, and OSF personnel. Maintenance phlebotomy to maintain control of iron stores will require a 8-hour DNIF/DNIC after each phlebotomy for RPA pilots, ATC and SWA personnel. Maintenance phlebotomy to maintain control of iron stores will require a 4-hour DNIF/DNIA after each phlebotomy for RPA sensor operator and MOD personnel. Per AFI, HH renders a member unfit for continued service, so does require an MEB.

**Table 1: Waiver potential for Hemochromatosis** 

| Flying Class (FC)     | Waiver Potential<br>Waiver Authority | ACS Review/Evaluation      |
|-----------------------|--------------------------------------|----------------------------|
| I/IA                  | No<br>AETC                           | No                         |
| II/III<br>ATC/GBO/SWA | Yes#*<br>AFMRA                       | At the discretion of AFMRA |

<sup>\*</sup>Initial FC II/III, ATC/GBO, and SWA requests for untrained individuals should be treated like FC I/IA and waiver should not normally be granted for a history of hemochromatosis.

#No indefinite waivers

AIMWITS search in Aug 2014 revealed a total of 27 submitted cases for the diagnosis of hemochromatosis. There were a total of 0 FC I/IA cases, 11 FC II cases, 13 FC III cases, 2 ATC/GBC cases, and 1 MOD case. There were 4 cases resulting in a disqualification and all 4 were FC III. One was an initial FC III which was disqualified for a history of PRK with an excessive preoperative refractive error, one was disqualified with new diagnoses of DM type I and hemochromatosis, another was disqualified for a history of a myocardial infarction, and the final one was disqualified for multiple medical issues.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for hemochromatosis should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of hemochromatosis including symptoms, pertinent negatives, complete physical and treatment plan.
- C. Consultation from a Gastroenterologist regarding need for liver biopsy if liver function tests abnormal or ferritin levels greater than 1000 ng/mL.
- D. Labs: Serum iron, serum ferritin, serum transferrin, and transferrin saturation; CBC; liver function tests to include ALT, AST, bilirubin, and alkaline phosphatase; fasting electrolytes and glucose levels; and thyroid function tests.
- E. Copy of all consults, imaging, and procedure reports.
- F. Genetic testing results (if done).
- G. ECG, echocardiogram, and Holter (reports, representative tracings, and echo tape should be sent to the ACS ECG library for FC II)
- H. MEB results

The AMS for <u>waiver renewal</u> for hemochromatosis should include the following:

- A. Interval history to include change in symptoms, medication usage, and side effects.
- B. All applicable labs and imaging tests as in the initial aeromedical summary. Individuals on maintenance phlebotomy should be followed with yearly serum transferrin saturation and ferritin. Further studies are dependent on symptoms.
- C. All consults since last AMS.
- D. All additional tests completed since last AMS.
- E. Results from most recent RILO, if an interval evaluation was performed.

## III. Overview.

Hemochromatosis is an iron overload syndrome first described by Trousseau in the French pathology literature in 1865. In 1889, von Recklinghausen gave the condition the name hemochromatosis because he thought that the disease was a blood disorder that caused increased skin pigmentation. In 1935, Sheldon published a description of all 311 cases of the disease that had been reported in the world's literature to that point, including several from his own records. He realized that hemochromatosis was an inborn error of iron metabolism and that all the pathologic manifestations of the disease were caused by increased iron deposition in the affected organs. In 1976, Simon and coworkers demonstrated that the gene for hereditary hemochromatosis (HH) was linked to the HLA region on the short arm of chromosome 6. The hemochromatosis gene was identified on chromosome 6 in 1996 and named HFE. C282Y is the major mutation of the HFE gene that is responsible for HFE related hereditary hemochromatosis. The second most common mutation in HFE is H63D.<sup>1,2</sup> Other gene mutations have been described that lead to hemochromatosis, but these are much rarer than the C282Y mutation.<sup>2, 3</sup> Studies by numerous investigators have shown that 80% to 90% of patients with typical features of HH are homozygous for the C282Y mutation.<sup>4,5,6</sup> Some people who are compound heterozygotes (C282Y/H63D) may also present with iron overload.<sup>1</sup>

Hemochromatosis is now known to be a genetic disease of autosomal recessive inheritance with a prevalence of approximately 1:250 in the US Caucasian population and is the most common genetic disease in populations of European ancestry. Population screening has demonstrated that the frequency of heterozygotes is 10 to 15% in the US Caucasian population and that the frequency is 0.5% (5 per 1000) for the homozygous state. The C282Y mutation is much less common in Hispanic, Asian American, Pacific Islander, and black persons. Due to incomplete penetrance of the C232Y mutation, a large number of individuals that are homozygotes for the mutation never develop clinically significant disease. Having the mutation only increases the risk for developing HH.

Adult men normally have 35 to 45 mg/kg of total body iron. Premenopausal women typically have lower iron stores, about 35 mg/kg due to the recurrent monthly blood loss that occurs with menstruation. More than two thirds of the body's iron content is incorporated into hemoglobin, and lesser amounts are found in muscle myoglobin (10-15%), enzymes and cytochromes (10%), with less than 1% circulating in plasma bound to transferrin. Under homeostatic conditions, the 1 to 2 mg of iron lost daily through sweat and sloughed cells of the skin and intestine is balanced by dietary iron absorption. There is no physiologic mechanism for the excretion of excess iron in humans, so the body stores are regulated by intestinal iron absorption in the duodenum. Improper regulation of this absorption can lead to iron overload, which is what occurs with HH. <sup>10, 11</sup>

Hepcidin is a peptide hormone that has an important role in iron homeostasis. It is secreted into circulation primarily by hepatocytes and helps to meet iron requirements by regulating iron absorption, mobilization, and storage. Hepcidin expression is up regulated by excess total body iron and inflammation which results in a decrease in iron absorption and lower amounts of iron released from macrophages. Hepcidin expression is down regulated by low total body iron, erythropoiesis, and hypoxia with a net result of more iron absorption and more iron released from macrophages. Hepcidin deficiency is the key mechanism of iron overload in the most commonly encountered forms of HH, in which gene mutations lead to defective or low hepatic synthesis of hepcidin for the degree of iron burden. Help is a peptide in the most commonly encountered forms of HH, in which gene mutations lead to defective or low hepatic synthesis of hepcidin for the degree of iron burden.

Most patients with HH become symptomatic at 40 to 50 years of age since most patients absorb only a few milligrams of excess iron daily. The clinical manifestations of disease often occur only after age 40 when body stores of iron have reached 15 to 40 grams (normal body iron stores are approximately 4 grams). Women can present later than men due to natural blood losses due to menstruation and child birth. When diagnosed at an advance stage, patients with HH often have the classic triad of cutaneous hyperpigmentation, diabetes, and cirrhosis. Currently, most patients are diagnosed prior to becoming symptomatic due to screening the family members of homozygous patients and the inclusion of iron studies on routine chemistry panels. Patients that do present with symptoms most often present with arthralgias, weakness, fatigue, hepatomegaly, and impotence. In patients with these types of presenting symptoms, serum iron studies to include serum iron, total iron-binding capacity (TIBC), serum transferrin, and transferrin saturation should be measured. HH should be suspected when the transferrin saturation is

above 45%. The serum ferritin is usually elevated in a person with HH but can be normal in young persons. In this setting, genetic testing should be strongly considered, looking for the HFE genotype. Similar genetic testing should be considered in first degree relatives of those known to have the disorder.<sup>1,9</sup>

In the past, HH could have devastating effects on those afflicted with the disorder. Excess iron leads to problems with the liver, heart, pancreas, gonads, thyroid gland, joints, and skin. Untreated disease can lead to hepatic cirrhosis, which accounts for about 85% to 90% of all HH-related deaths. Individuals with HH and cirrhosis can have up to a 5% annual risk for developing hepatocellular carcinoma, a 200 fold increase. 11 Hemochromatosis patients who drink in excess of 60 grams of alcohol daily are approximately nine times more likely to develop cirrhosis than are those who drink less than this amount. Therefore, it is strongly recommended that HH patients decrease or eliminate alcohol consumption.<sup>14</sup> Hemochromatosis can also result in a mixed dilatedrestrictive or dilated cardiomyopathy and conduction disturbances. Cardiac dysrhythmias and cardiomyopathies are the most common cause of sudden death in iron overload states. Iron excess can lead to diabetes by either iron accumulation in the pancreatic beta cells or by impairing insulin sensitivity. Hypogonadism is the most common nondiabetic endocrinopathy and can present as impotence, amenorrhea, decreased libido, or osteoporosis. Thyroid dysfunction in HH occurs at a rate approximately 80 times over the rate in unaffected men. Classic HH arthropathy occurs in up to 50% of patients and resembles noninflammatory osteoarthritis. Skin pigment changes often present as a "bronzing", but can be brown or slate-gray as well. 11

Phlebotomy has long been the standard treatment for HH. Each unit (400-500 mL) of whole blood removed contains 200 to 250 mg of iron. In providing replacement for the hemoglobin lost during the phlebotomy, the body mobilizes an equal amount of iron from tissue stores, which reduces the degree of iron overload. For a patient diagnosed with HH who has an excess of 10 grams in iron stores, one phlebotomy per week for 50 weeks should fully deplete the accumulated iron stores. An endpoint for weekly phlebotomies is normalized iron stores, defined as a serum ferritin <50 ng/mL and transferrin saturation <50%. A maintenance phlebotomy schedule should then be continued following the primary iron depletion to prevent reaccumulation. Most clinicians agree that the goal is to keep the ferritin concentration between 50 and 100 ng/mL or less. For maintenance, most patients require a 500 mL phlebotomy every two to four months.<sup>1,9,15</sup> It is now widely recognized that the prognosis of HH depends on the amount and duration of excess iron. Early diagnosis and prompt therapy largely prevent the adverse consequences of the disease and essentially normalize life expectancy.<sup>16</sup>

As with all diseases with a known genetic cause, there are questions regarding mass screening in order to diagnose early and treat prior to the patient becoming symptomatic. At this time, large-scale screening is not recommended as there are unanswered questions regarding cost-effectiveness.<sup>2, 17</sup> On the other hand, all first-degree relatives should be offered testing once an HH proband is diagnosed. If an adult relative of a C282Y homozygote is identified, and is either a C282Y homozygote or a compound heterozygote (C282Y/H63D) and if blood iron studies are abnormal then a presumptive diagnosis can

be made and therapeutic phlebotomy can be initiated. Early treatment can prevent complications.

Dietary supplements containing iron should be avoided. It may be reasonable to recommend avoidance of vitamin C supplements due to their possible enhancement of free iron and the generation of reactive oxygen species.

## IV. Aeromedical Concerns.

Hemochromatosis has the potential to affect numerous organ systems of the body through the deposit of iron in the tissue. Some of the major aeromedical concerns include: 1) cardiac arrhythmias or cardiomyopathy, 2) manifestations of cirrhosis of the liver and hepatocellular carcinoma, such as altered mental status and hemorrhage, and 3) diabetes mellitus. Arthropathy could become severe enough to interfere with controlling the aircraft. Symptoms of hypogonadism and hypothyroidism would be of gradual onset and not likely to be suddenly incapacitating. Treatment compatible with flying (phlebotomy) is available, as long as the appropriate post-phlebotomy period is observed.

| ICD-9 code for Hemochromatosis |                              |
|--------------------------------|------------------------------|
| 275.0                          | Disorders of iron metabolism |

| ICD-10 code for Hemochromatosis |   |
|---------------------------------|---|
| E83.10                          | Disorders of iron metabolism, unspecified |

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#### **WAIVER GUIDE**

Updated: Jun 2016

Supersedes Waiver Guide of Apr 2013

By: Maj Andrew Timboe (RAM 17) and Dr Dan Van Syoc

Reviewed by Col Pat Storms, RAM 05 and AF/SG consultant for Gastroenterology

## **CONDITION:**

Hepatic Cirrhosis (Jun 2016)

## I. Waiver Consideration.

The diagnosis of hepatic cirrhosis is disqualifying for all flying classes, ATC, GBO and SWA duties as well as retention.

**Table 1: Waiver potential for hepatic cirrhosis** 

| Flying Class (FC) | <b>Waiver Potential</b> | ACS Review/Evaluation    |
|-------------------|-------------------------|--------------------------|
|                   | Waiver Authority        |                          |
| I/IA              | No                      | No                       |
|                   | AETC                    |                          |
| II/III            | Initial - No            | No                       |
|                   |                         |                          |
|                   | Maybe*+!                | Yes                      |
|                   | MAJCOM                  |                          |
| ATC/GBO/SWA       | Initial - No            | No                       |
| MOD               |                         |                          |
|                   | Maybe*+!                | At the discretion of the |
|                   | MAJCOM                  | waiver authority         |

<sup>\*</sup> Waiver possible with documentation of treatment and resolution of symptoms or documentation of adequate control measures.

AIMWTS search in Jun 2016 revealed a total of 48 cases with a diagnosis of cirrhosis. Breakdown of cases was as follows: 1 FC I/IA case (not disqualified), 24 FC II cases (5 disqualified), 19 FC III cases (3 disqualified), 4 ATC/GBC cases (0 disqualified), and 0 MOD cases. All 8 disqualified cases were either due to severe disease or for multiple medical problems.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>+</sup> MEB required first if subspecialty follow-up is required or if there are complications, to include abnormal liver function; waiver authority then becomes AFMRA.

<sup>!</sup> No indefinite waiver.

The AMS for the <u>initial waiver</u> for hepatic cirrhosis should include the following: A. Complete history with clear delineation of the underlying disease process that led to the development of cirrhosis, and notation of the presence or absence of major complications of hepatic cirrhosis to include ascites, any episodes of spontaneous bacterial peritonitis, varices with or without bleeding, hepatic encephalopathy, and any other medical complications attributed to the diagnosis of cirrhosis. Document any alcohol use: years, amount, and if still drinking.

- B. Exam: Vital signs, weight (as many as possible to assess fluid gains from ascites if present), thorough abdominal and neuromuscular exams.
- C. Labs: CBC with platelet count, metabolic panel with liver function tests, lipid panel, PT/PTT, iron panel, ceruloplasmin with serum copper level and urine copper levels, serum protein electrophoresis, 24 hour urine protein, alpha 1-antitrypsin level, antinuclear antibody, complete viral hepatitis panel, anti-mitochondrial antibody, and anti-smooth muscle antibody.
- D. Imaging studies: CT-scan of the liver, ultrasound of the abdomen, radionuclide liver/spleen scan or as clinically recommended by consultant.
- E. Reports of any endoscopic examinations.
- F. Pathology reports from any biopsies.
- G. Consultation reports from a gastroenterologist or hepatologist.
- H. If alcohol dependent, report from ADAPT and documentation that aviator will remain abstinent. Refer to Alcohol Abuse and Dependence waiver guide for assistance.
- I. Medical treatments: all drugs used to include dosages and any side effects.
- J. Medical evaluation board results (if required).

The AMS for <u>waiver renewal</u> for hepatic cirrhosis should include the following:

- A. Interval history and focused exam.
- B. All applicable labs, pathology reports, and imaging tests noted above.
- C. Consultation report from a gastroenterologist or hepatologist.

## III. Overview.

According to the National Center of Health Statistics, chronic liver disease and liver cirrhosis account for 11.5 deaths per 100,000 people in the United States making it the 12<sup>th</sup> most common cause of death. Cirrhosis in Greek means orange or tawny, and was definitively described by Laennec over a century and a half ago. Hepatic cirrhosis is defined as a chronic disease of the liver in which diffuse destruction and regeneration of the hepatic parenchymal cells have occurred, and in which a diffuse increase in connective tissue has resulted in disorganization of the lobular and vascular architecture. The most common etiologies for cirrhosis in the United States are from chronic Hepatitis C virus and alcohol-related liver disease; however the incidence of non-alcoholic fatty liver disease (NAFLD) is on the rise due to increased rates of obesity. Other causes include primary biliary cirrhosis (PBC), autoimmune hepatitis, drug-induced liver injury, hemochromatosis, celiac disease, alpha-1-antitrypsin deficiency, Wilson's disease, sarcoidosis, protozoan infection, small bowel bypass, a variety of lesser miscellaneous causes, and cryptogenic cirrhosis. The distribution of causes of cirrhosis in a military population is not well-described, nor is the distribution of causes in a population of

military aviators. Worldwide, the prevalence of chronic liver disease or cirrhosis is estimated to be 100 per 100,000, but it varies widely by country and by region.<sup>4</sup>

Two conditions warrant particular consideration in a population of generally young healthy aviators: NAFLD and autoimmune hepatitis. NAFLD is increasingly common, and reflects a spectrum that ranges from simple fatty liver without inflammation, to non-alcoholic steatohepatitis (NASH) that can result in cirrhosis and liver failure. The apparent correlation between weight gain, metabolic syndrome and NAFLD increases concern about this condition in the face of our obesity "epidemic". Autoimmune hepatitis is a progressive chronic hepatitis that can impact both adults and children. It can share features with other immune-based inflammatory liver conditions, including primary biliary cirrhosis and sclerosing cholangitis. Potential triggers include drugs and viral infections, and it is felt that "aberrant autoreactivity" plays a role. Both NAFLD and autoimmune hepatitis can strike an otherwise healthy military aviator, and are thus important to understand in detail.

Liver dysfunction in the face of cirrhosis is manifest as both synthetic dysfunction and vascular pressure concerns. Signs and symptoms are myriad, depending on the severity and underlying cause of the cirrhosis. Constitutional symptoms often include "failure to thrive", with wasting, anorexia, weakness and fatigue.<sup>2</sup> Jaundice may be noted in the face of end-stage synthetic dysfunction or biliary obstruction, and physical exam findings aside from jaundice may include palmar erythema, thenar wasting, Caput Medusae, and ascites. A patient with advanced cirrhosis and hepatic encephalopathy may demonstrate decreased mental status to the point of coma, and reveal asterixis on physical exam. And of course a dramatic presentation with aggressive gastrointestinal hemorrhage from variceal rupture may drive a physician's initial encounter with a cirrhotic patient. The two main consequences of hepatic cirrhosis are portal hypertension and liver insufficiency.<sup>4</sup>

Laboratory assessment of the cirrhotic patient often reflects the severity of their hepatic dysfunction. Elevated transaminases suggest ongoing hepatocyte destruction. Anemia can reflect either active or recent bleeding, or can be a result of the "anemia of chronic disease". Thrombocytopenia is common in the advanced cirrhotic, due to both sequestration and decreased production. Hyperbilirubinemia can be the result of drastically reduced hepatic reserve, or can be a marker of biliary obstruction at the intra or extra-hepatic level. Radiologic assessment may include sonographic evidence of a small echogenic liver, enlarged spleen, and, in the case of biliary obstruction, dilated biliary radicals. A radioisotope liver scan will often reveal decreased uptake in the hepatic bed with shunting of the radionuclide into an enlarged, bright spleen. CT scan is of considerable value in assessing the patient for one of the very serious complications of cirrhosis: hepatocellular carcinoma. Of course, liver biopsy is the definitive method to assess for the presence of cirrhosis and to gain valuable information about the potential underlying cause of the cirrhosis. Unfortunately, the risks of liver biopsy in the cirrhotic patient with ascites and coagulopathy can be considerable. Recently, the "Fibroscan", a non-invasive method of determining liver stiffness, has gained attention as a tool to assess for cirrhosis without the need to resort to liver biopsy. 8, 9 Interest in developing serologic

panels or algorithms to assess for the presence of hepatic fibrosis/cirrhosis is considerable, but such panels and algorithms are not yet been established as standards of care. 10

## Treatment

Treatment of hepatic cirrhosis is less about reversing established hepatic fibrosis than it is about reducing or eliminating ongoing hepatocyte destruction, preserving residual functional capacity, and treating the complications of established cirrhosis. 11 Therapy to reduce hepatocyte destruction depends on the primary disease process. In patients with chronic Hepatitis C virus (HCV), antiviral therapy is complex and quickly changing and now even boasts treatments with interferon-free regimens. All cirrhotic patients with HCV should undergo quantitative HCV RNA and genotype before initiating antiviral therapy. 12 For patients with alcoholic cirrhosis, abstinence remains the cornerstone of therapy. Those with NAFLD should pursue vigorous controlled weight loss. For patients with primary biliary cirrhosis and primary sclerosing cholangitis, ursodeoxycholic acid (UDCA) has demonstrated an ability to slow down disease progression and reduce the severity of cholestatic symptoms. In hemochromatosis, regular therapeutic phlebotomy remains the treatment mainstay, whereas patients with Wilson's disease should be treated with chelation therapy. 13, 14 Treatment of the underlying liver disease, before the development of cirrhosis, is a primary prevention strategy. As the major causes of cirrhosis are related to lifestyle choices, primary prevention programs that focus on encouraging alcohol abstinence, reducing high-risk behavior for hepatitis virus infection, and vaccinating for hepatitis B are proven prevention strategies.<sup>4</sup>

Beyond the disease-specific considerations discussed above, there is some evidence that established drugs, such as non-selective beta blockers (NSBBs), statins, antibiotics, and anticoagulants might have expanded application in patients with cirrhosis regardless of etiology, and that these agents could prevent or delay the advent of complications. NSBBs are effective in both primary and secondary prevention of variceal bleeding, regardless of the etiology of cirrhosis. Broad spectrum antibiotics such as quinolones and, recently, rifaximin, have been shown to have value in primary and secondary prevention of spontaneous bacterial peritonitis in cirrhotic patients. Statins have been shown to reduce portal hypertension, and in a large population of cirrhotics with diabetes were found to reduce the risk of hepatocellular carcinoma. Finally, while anticoagulation is currently used only for limited indications such as portal vein thrombosis, its use preemptively may reduce the development of portal vein thrombosis and potentially even impact the progression of fibrosis.<sup>15</sup>

## IV. Aeromedical Concerns.

Aeromedical concerns include: torrential gastrointestinal hemorrhage, hepatic encephalopathy, generalized malaise and lethargy, metabolic bone disease, ascites, renal dysfunction and pulmonary decompensation. Each of the underlying medical conditions may have additional aeromedical concerns, such as itching related to PBC. As many of the cirrhotics in our aviation population will have problems with alcohol, there are also concerns related to alcohol use/abuse and the behavior associated with this condition.

In the face of portal hypertension, gastric or esophageal varices could result in spontaneous massive upper GI hemorrhage, and while a literature search failed to reveal studies evaluating the risk of the anti-G straining maneuver in patients with portal hypertension, it would seem unwise for patients with varices to engage in this vigorous activity. Aggressive gastrointestinal hemorrhage could certainly lead to sudden incapacitation and unconsciousness.

Hepatic encephalopathy would be hazardous for aircrew duties due to compromised cognition, impaired higher executive decision making and decreased dexterity. Ascites could interfere with proper fit and function of the anti-G suit, and the anorexia and inanition that are often found in cirrhotic patients undermine proper conditioning necessary for top physical performance while flying. Finally, hepatopulmonary syndrome and portopulmonary hypertension could potentially lead to hypoxemia.

| ICD-9 codes for hepatic cirrhosis |  |
|-----------------------------------|--|
| 571                               | Chronic liver disease and cirrhosis                              |
| 571.0                             | Alcoholic fatty liver  |
| 571.2                             | Alcoholic cirrhosis of liver, including Laennec's cirrhosis      |
| 571.5                             | Cirrhosis of liver without mention of alcohol (portal cirrhosis, |
|                                   | cryptogenic, postnecrotic, post hepatic, NOS                     |
| 571.6                             | Biliary cirrhosis  |
| 571.8                             | Other chronic nonalcoholic liver disease (NAFLD)                 |

| ICD-10 codes for hepatic cirrhosis |  |
|------------------------------------|--|
| K70.0                              | Alcoholic fatty liver                        |
| K70.30                             | Alcoholic cirrhosis of liver without ascites |
| K70.31                             | Alcoholic cirrhosis of liver with ascites    |
| K74.60                             | Unspecified cirrhosis of liver               |
| K74.69                             | Other cirrhosis of liver                     |
| K74.5                              | Biliary cirrhosis, unspecified               |
| K75.81                             | Nonalcoholic steatohepatitis (NASH)          |

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### WAIVER GUIDE

Updated: Jul 2013

Supersedes Waiver Guide of Aug 2009

By: Lt Col Talib Y. Ali (RAM 13) and Dr. Dan Van Syoc Reviewed by Col Pat Storms, RAM 05 and gastroenterologist

## **CONDITION:**

Hepatitis, Viral (Jul 2013)

## I. Waiver Considerations.

Chronic viral hepatitis is disqualifying for all flying classes in the US Air Force. Specifically, for FC I/IA/II/III "History of viral hepatitis, with carrier status, persistent transaminase elevation, or evidence of chronic active or persistent hepatitis is disqualifying." For retention: "chronic, when symptoms persist after a reasonable time following the acute stage and there is objective evidence of impairment of liver function or if member requires follow up/treatment beyond six months and any other chronic liver disease whether congenital or acquired." Waiver consideration will hinge upon the severity of hepatic inflammation, functional hepatic capacity, and absence of significant neuropsychiatric symptoms.

AFMSA/SG3PF granted a waiver for the use of Entecavir for chronic active hepatitis in an exchange pilot. A waiver was recommended and requested by the AF/SG of his country. AFMRA honored this waiver IAW a long standing STANAG (Standardization Agreement) policy. Both the condition and treatment remain disqualifying in the USAF.

Table 1: Waiver Potential for Hepatitis B or C for FC I/IA, FC II and FC III

| Flying Class | Waiver Potential | ACS                  |
|--------------|------------------|----------------------|
| (FC)         | Waiver Authority | Review/Evaluation    |
| I/IA         | No               | Only if requested by |
|              | AETC/SGPS        | AETC/SGPS            |
| II/III       | Maybe*+#         | Yes                  |
| ATC/GBO/SWA  | MAJCOM           |                      |

<sup>\*</sup> Waiver possible with resolution acute phase and no sequelae from chronic state.

Review of AIMWTS waiver submissions for viral hepatitis in Jul of 2013 showed 67 waivers submitted for Hep B and Hep C. Breakdown of the cases was as follows: 4 FC I/IA (2 disqualified), 23 FC II (0 disqualified), 36 FC III (10 disqualified), and 4 ATC/GBC (2 disqualified). There were a total of 14 submissions that resulted in a disqualification.

<sup>+</sup> MEB required first for evidence of persistent liver impairment.

<sup>#</sup> No indefinite waiver.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for hepatitis should include:

- A. History, including diagnosis, comprehensive serology results related to the specific viral infection being considered (if any), all available chronological LFT results, treatments, if any, and current performance at work (particularly with regard to possible fatigue or neuropsychiatric symptoms).
- B. List and fully discuss all clinical diagnoses requiring a waiver.
- C. Results of physical examination, focusing on signs of acute and chronic liver disease.
- D. Gastroenterology/hepatology evaluation.
- E. Current LFTs, serum albumin, prothrombin and CBC with platelet count.
- F. MEB report (if required under 5B 5.3.9.6.).
- G. A liver biopsy need not be routinely performed prior to waiver request, although the waiver authority may ask for this in specific cases.

The AMS for <u>waiver renewal</u> for hepatitis should include the following:

- A. Interim history to include documentation recent serology and LFTs, and work performance. Other labs should include serum albumin, prothrombin time, and CBC.
- B. Current treatment if applicable.
- C. Results of each annual examination, focusing on signs of acute and chronic liver disease.
- D. Gastroenterology evaluation (internal medicine evaluation will suffice if patient has been stable for over twelve months).

At this time, each of the medications listed in Table 1 for hepatitis immunotherapy/ chemotherapy is disqualifying. Waivers may be considered on a case-by-case basis for patients with viral hepatitis before or after treatment, and will depend on the status of the underlying disease and must meet the waiver criteria outlined in AFI 48-123.

## III. Overview.

Hepatitis (hepatocellular inflammation) can result from many types of infectious agents (including bacterial, protozoan, and viral organisms), alcohol, drugs, dietary supplements, chemicals, and metabolic or autoimmune processes. The most common infectious agents of the liver that the flight surgeon likely will encounter are viral. Hepatitis A, B, C, D, E and G have been described. These viral hepatitides are divided based upon their mode of transmission – enteral (Hepatitis A and E) or parenteral (Hepatitis B, C, D, and G). Other viruses such as herpes simplex, Epstein-Barr virus (EBV), mumps, rubella, rubeola, adenovirus, coxsackie virus, and yellow fever virus can cause inflammation of the liver but are not a primary causes of hepatitis. Acute viral hepatitis is a spectrum of clinical disease ranging from asymptomatic infections, marked only by a rise in aminotransaminase levels, to fulminant hepatic necrosis and failure. Symptoms during the

acute phase of a viral hepatitis episode may include anorexia, nausea, vomiting, fatigue, malaise, arthralgias, myalgias, headache, jaundice, abdominal discomfort, and constitutional symptoms often described as a "flu-like illness." Symptom expression is variable and asymptomatic infections are 10 to 30 times more common than symptomatic viral hepatitis infections. Accurate diagnosis is important for future waiver actions, and patients should have clinically appropriate medical care and evaluation through the acute phase of any hepatitis regardless of etiology. The focus of the remainder of this waiver guide will be on Hepatitis B (HBV) and Hepatitis C (HCV) viruses. However with the advent of a universal vaccination program, the prevalence of Hepatitis B in the United States Armed Forces has decreased.

Generally, patients will achieve full functional recovery from an acute viral hepatitis with minimal clinical sequelae, with only a few patients progressing to acute hepatic failure. Recovery from the acute phase of viral hepatitis can be assumed when symptoms have resolved, liver enzymes have normalized, and viral markers demonstrate a pattern of resolution or of persistent chronic infection—usually within six months of the initial infection. With immunologic clearance of a HBV infection, surface antigenemia will usually resolve after three months. Chronic infection is likely if the viral surface antigen is still detectable after six months. Approximately 5% of immunocompetent adults will become chronically infected following an acute case of HBV. Figure 1 demonstrates the typical time course of viral serologies following an HBV infection.<sup>1</sup>

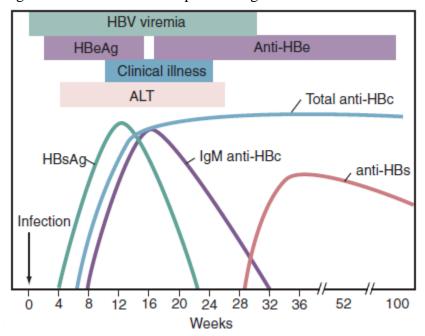


Figure 1: Time course of Hep B serologies

In cases of chronic HCV infection, the acute phase often is subclinical and not identified. A persistent, detectable viral load indicates chronic infection and 85% of HCV infections will become chronic. Up to 15% of patients with chronic hepatitis C also have extrahepatic manifestations often associated with autoimmune or lymphoproliferative

states like lichen planus, idiopathic thrombocytopenic purpura, thyroid abnormalities and diabetes.<sup>2</sup>

Chronic infections with either of these viruses may be static or indolent with minimal demonstrable sequelae. Conversely, chronic viral hepatitis can result in hepatocellular carcinoma, cirrhosis, or end-stage hepatic failure requiring liver transplantation.<sup>3</sup> In chronic HBV infection antigen-antibody immune complexes may persist and cause arthralgias, arthritis, glomerulonephritis and polyarteritis. In HCV, chronic hepatitis may not progress, or may progress in a slow and insidious fashion. Progression to cirrhosis may develop in up to 15-30% of chronically infected HCV patients. Progression tends to be slower (over 30 years) for females who were younger at age of first infection, and is accelerated in all patients in the presence of alcohol use or infection with other hepatopathic agents. Once cirrhosis is present, hepatocellular carcinoma may occur at a rate of 1-3% per year.<sup>3</sup> A liver biopsy is a useful tool to stage the current status of hepatic inflammatory activity and fibrosis, and may help direct appropriate therapy, but should not be considered necessary in every case of chronic HCV infection.<sup>2</sup> Please note that the historical distinction between "chronic active" and "chronic persistent" hepatitis C has fallen out of favor, consistent with the observation that chronic viral hepatitis presents with a spectrum of histologic and clinical manifestations, and treatment decisions hinge on serologic, histologic, and functional findings.

Pharmaceutical therapy is available for chronic B and C virus hepatitis but these drugs have significant side effects. Specific treatment regimens are beyond the scope of this document, but it is important to note that recent advances in the development of direct-acting antiviral agents have dramatically increased the viral clearance rate in chronic hepatitis C, from less than 10% with the initial regimen of interferon monotherapy to more than 70% with current therapy<sup>4</sup>. It is also worth noting that, in the case of chronic hepatitis C, the genotype (1-6) of the strain of the virus can impact response to therapy and should be taken into consideration when considering treatment regimens.<sup>4</sup>

Table 2: Treatment regimens for Hepatitis B and Hepatitis C

|             | Treatment Agent    | Potential side effects <sup>1, 5</sup>                 |
|-------------|--------------------|--|
| Hepatitis B | Interferon-α-2a    | Headache, fever, fatigue, thrombocytopenia,            |
|             | Peginterferon-α-2a | anorexia, insomnia, demotivation, depression,          |
|             |                    | paranoia, diabetes mellitus, optic neuritis, seizures, |
|             |                    | cardiotoxicity   |
|             | Lamivudine         |  |
|             | Adefovir           | Headaches, nausea, vomiting, dizziness, insomnia,      |
|             | Entecavir          | lactic acidosis, exacerbation of viral hepatitis,      |
|             | Telbivudine        | pancreatitis, cough, rashes, arthralgias               |
|             | Tenofovir          |  |
| Hepatitis C | Peginterferon-α-2a | Headache, fever, fatigue, thrombocytopenia,            |
|             |                    | anorexia, insomnia, demotivation, depression,          |
|             |                    | paranoia, diabetes mellitus, optic neuritis, seizures, |
|             |                    | cardiotoxicity   |
|             | Ribavirin          | Hemolysis, nausea, anemia, pruritus, gout              |
|             | Telaprevir         | Anemia, rash, anorectal discomfort                     |
|             | Boceprevir         | Anemia, neutropenia, dysgeusia                         |

For both infections, the risks and benefits of treatment with antivirals must be weighed against the current clinical state and likelihood of disease progression. Treatment is typically reserved until there is evidence of chronic liver disease (as demonstrated by unequivocal serological and laboratory results, or biopsy results showing moderate necrosis and inflammation, or definite fibrosis) rather than empirically treating virological carrier status.<sup>2, 4, 5</sup> With the advent of more effective antiviral therapy for chronic hepatitis C, however, the future may hold a reality in which chronic hepatitis C is treated more like an infection to be addressed with specific antiviral therapy than as a chronic liver disease.

#### IV. Aeromedical Concerns.

Aviators with acute hepatitis are unfit to fly due to the likelihood of unacceptable symptoms, as are those with chronic hepatitis who are either undergoing drug treatment or who have demonstrated functional impairment due to their chronic liver disease. However, aviators who have fully recovered from an episode of acute viral hepatitis, as demonstrated by being asymptomatic with liver function tests (LFTs) within the standard reference range and negative viral markers, may be returned to flying status without requiring a waiver. Careful consideration must be given to the time course of viral markers, as their evolution may occur over weeks to months.

Aviators with chronic viral hepatitis may experience many years without functional impairment before the onset, if at all, of aeromedically significant complications. Therefore, individuals may be considered for a waiver if they are off disqualifying medications, demonstrate normal hepatic functional capacity and have no significant symptoms of hepatic decompensation or extrahepatic manifestations of chronic hepatitis. Aviators suspected to be chronic carriers should be evaluated similarly to those with chronic viral hepatitis, though additional consideration should be given to any particular

occupational hazards associated with blood and body fluid exposure from the chronic carrier. Due to the high risk of chronicity, HCV-infected aviators should be under the clinical care of a gastroenterologist.

| ICD-9 Cod | ICD-9 Codes for Viral Hepatitis                                 |  |  |
|-----------|---|--|--|
| 070       | Viral Hepatitis NOS   |  |  |
| 070.1     | Viral hepatitis A without mention of hepatic coma               |  |  |
| 070.3     | Viral hepatitis B without mention of hepatic coma               |  |  |
| 070.5     | Other specified viral hepatitis without mention of hepatic coma |  |  |
| 070.52    | Hepatitis delta without mention of hepatitis B w/ hepatic coma  |  |  |
| 070.6     | Unspecified viral hepatitis with hepatic coma                   |  |  |
| 070.70    | Viral Hepatitis C without mention of hepatic coma               |  |  |
| 070.9     | Unspecified viral hepatitis without hepatic coma                |  |  |

| ICD-10 Co | ICD-10 Codes for Viral Hepatitis                   |  |  |
|-----------|--|--|--|
| B17.9     | Acute viral hepatitis, unspecified                 |  |  |
| B18.9     | Chronic viral hepatitis, unspecified               |  |  |
| B15.9     | Hepatitis A without hepatic coma                   |  |  |
| B19.10    | Unspecified viral hepatitis B without hepatic coma |  |  |
| B19.0     | Unspecified viral hepatitis with hepatic coma      |  |  |
| B17.10    | Acute hepatitis C without hepatic coma             |  |  |
| B19.20    | Unspecified viral hepatitis C without hepatic coma |  |  |
| B19.9     | Unspecified viral hepatitis without hepatic coma   |  |  |

## V. References.

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# Herniated Nucleus Pulposus (HNP) and Spinal Fusion (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), Lt Col James Dunlap (AF Ortho Spine Specialist), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

Updated Waiver Considerations, Tables 1-3, Aeromedical Concerns and References

#### I. Waiver Consideration

A history of HNP or surgery for it is disqualifying for FC I/IA/II/III and requires a waiver under MSD K6. All flying classes and OSD personnel require a waiver when they fall under MSD K5: "Herniation of nucleus pulposus, when symptoms and associated objective findings are of such a degree as to require repeated hospitalization, significant duty limitations, or frequent absences from duty." MSD K5 is disqualifying for retention standards, so would also require an MEB or RILO. <u>If surgical intervention is contemplated, note that cervical disc arthroplasties (artificial disc replacements) are not routinely aeromedically-approved for high-performance aircraft operation waiver, and may also be duty-limiting for personnel on jump status.</u>

Aviation personnel must fulfill all of the following applicable qualifying criteria for the initial waiver request:

- Need to be asymptomatic or with non functionally-limiting symptoms or signs
- Need to have adequate waiting period after treatment see Table notes
- Please note difference in waiting times for different categories.

Table 1: Waiver potential for HNP treated conservatively, or surgically without fusion or disc replacement

| tubion of tube replacement |                    |                  |                  |
|----------------------------|--------------------|------------------|------------------|
| Flying Class               | Waiver             | Waiver Authority | ACS Review or    |
| (FC)                       | Potential          | waiver Authority | Evaluation       |
| FC I/IA                    | No                 | AETC             | No               |
| FC II                      | Yes <sup>1,2</sup> | MAJCOM           | Yes <sup>3</sup> |
| FC III                     | Yes <sup>1,2</sup> | MAJCOM           | No               |
| ATC, GBO,                  | Yes <sup>1</sup>   | MAJCOM           | No               |
| SWA                        | 168                | MAJCOM           | INO              |

- 1. Minimum observation period post-treatment: 6 months if on jump status, otherwise 3 months
- 2. Multi-level cervical spine surgery waivers restricted to non high-performance aircraft
- 3. For cases with over 4 years stability, ACS review is not required, and is at the discretion of the waiver authority

Table 2: Waiver potential for HNP treated with spinal fusion, with or without hardware

| Flying Class (FC) | Waiver<br>Potential | Waiver Authority | ACS Review or<br>Evaluation |
|-------------------|---------------------|------------------|-----------------------------|
| FC I/IA           | No                  | AETC             | No                          |
| FC II             | Yes <sup>1,2</sup>  | MAJCOM           | Yes <sup>3</sup>            |
| FC III            | Yes <sup>1,2</sup>  | MAJCOM           | No                          |
| ATC, GBO,<br>SWA  | Yes <sup>1</sup>    | MAJCOM           | No                          |

- 1. Minimum observation period post-treatment: 6 months for FC II, 4 months for FC III/GBO
- 2. Multi-level cervical fusion waivers restricted to non high-performance aircraft
- 3. For cases with over 4 years stability, ACS review is not required, and is at the discretion of the waiver authority

Table 3: Waiver potential for HNP treated with artificial disc replacement

| Flying Class (FC)        | Waiver<br>Potential | Waiver Authority | ACS Review or Evaluation |
|--------------------------|---------------------|------------------|--------------------------|
| FC I/IA                  | No                  | AETC             | No                       |
| FC II                    | Yes <sup>1</sup>    | AFMRA            | Yes <sup>2</sup>         |
| FC III, ATC,<br>GBO, SWA | Yes <sup>1</sup>    | AFMRA            | Yes <sup>2</sup>         |

- 1. Minimum observation period post-treatment: 6 months
- 2. Cervical disc arthroplasty waivers currently routinely restricted to non high-performance aircraft

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. Detailed history of back/neck pain and previous treatments; surgical history; any specialty consultative reports and follow-up notes.
- 2. Current physical, musculoskeletal (spinal) and neurological examinations.
- 3. Operative report (if surgically treated).
- 4. Consultant statement clearing member for unrestricted activities or flying duties
- 5. Follow-up dynamic (flexion-extension) radiographs to confirm stability if treated with spinal fusion, instrumentation, hardware or disc replacement.
- 6. Reports and images from all relevant imaging studies performed. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- Interval history, to include any residual signs and symptoms, current symptoms, current medications, current treatment, current pain level, and any activity limitations.
- 2 Physical musculoskeletal (spinal) and neurological exam.
- 3 Copies of any interim specialty consultations, follow-up notes, imaging studies and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## **III. Aeromedical Concerns**

Aeromedical concerns include effects of any current symptoms or signs on operational safety and mission effectiveness, and future risk of symptom development, especially with stressors of high-performance aircraft operations or aircraft ejection, which could be of sudden onset and severe intensity. Following surgical treatment of HNP, concerns also include potential for vertebral joint stability and hardware failure. There are documented cases of disc herniations, vertebral fractures, and neck injuries with high-G maneuvers and ejections. After spinal fusion, there is concern over the possibility of repeat injury to a fused spine as a result of ejection and rapid-onset Gz-forces. The normal acceleration magnitude during ejection from the ACES II seat is 12-14 +Gz, but may vary with flight parameters and weight of occupant. Parachute opening shock can range from 10 to 20 +Gz, especially if outside the ejection envelope. Vertebral fracture occurs frequently with forces of greater than 20 +Gz, but with poor positioning, forces as low as 10 +Gz have caused fractures. Non-waiverability of multi-level cervical fusions for high-performance and ejection seat aircraft is based on the concern of increased stress concentration at adjacent non-fused vertebral joints during flexion, extension, and rotation. Multi-level lumbar or thoracic fusions may be considered for waiver in ejection seat aircraft as the thoracolumbar joints are not generally as mobile as the cervical joints, resulting in less severe focal stress concentrations at adjacent non-fused levels, and a lumbar fracture or other injury is far less likely to result in permanent neurological impairment. In cases of fusion, it is essential to establish successful complete fusion prior to consideration of returning to fly, particularly in high-performance aircraft operations. This can take up to 12 months in some cases. Artificial disc replacement devices have not been adequately assessed for stability with anticipated stressors experienced in high-performance aircraft operations, and cervical spine disc arthroplasties are currently not routinely recommended for such waivers. Further studies are needed to demonstrate equivalence or superiority of disc arthroplasty vs. fusion in both cervical and lumbar regions, and studies demonstrating device stability under sustained high-performance aircraft operation conditions.

AIMWTS search in Mar 2019 revealed 838 members with a diagnosis of HNP and/or spinal fusion since Jan 2014. There were 97 cases resulting in disqualification. Breakdown of the cases demonstrated: 13 FC I/IA cases (8 disqualified), 442 FC II cases

(30 disqualified), 18 RPA pilot cases (1 disqualified), 344 FC III cases (50 disqualified), 19 ATC/GBC cases (8 disqualified), and 2 MOD cases (0 disqualified).

| ICD-9 Codes for HNP and Spinal Fusion |  |  |
|---------------------------------------|--|--|
| 722                                   | Intervertebral Disc Disorders            |  |
| 81.0                                  | Spinal Fusion                            |  |
| 81.3                                  | Refusion of Spine                        |  |
| 84.60                                 | Insertion of Spinal Disc Prosthesis, NOS |  |

| ICD-10 Codes for HNP |   |
|----------------------|---|
| M50.20               | Other cervical disc displacement unspecified cervical |
|                      | region  |
| M51.26               | Other intervertebral disc displacement, lumbar region |

## IV. Suggested Readings

- 1. Rayman RB. *Rayman's Clinical Aviation Medicine*, 5th Ed., Castle Connolly Graduate Medical Publishing, LTD, 2013; 293-94.
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- 5. Gao S, Geng X, Fang Q. Spontaneous disappearance of large lumbar herniation. JAMA Neurology 2018; 75(1):123-124.
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- 7. Robinson J, Kothari MJ. Treatment and prognosis of cervical radiculopathy. UpToDate, Aug 31, 2018.
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### WAIVER GUIDE

Updated: May 2015

Supersedes Waiver Guide of Apr 2012

By: Maj Jennifer Wolf (RAM 16) and Dr. Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

## **CONDITION:**

Hodgkin Lymphoma (May 2015)

## I. Waiver Considerations.

History of Hodgkin lymphoma (HL)is disqualifying for all flying classes. In addition, all malignancies require an I-RILO no more than 90 days after the start of treatment, which necessitates a waiver for all ATC/GBO and SWA personnel with HL who are returned to duty.

Table 1: Waiver potential for various stages of Hodgkin lymphoma and flying class.

| Flying Class (FC) | Condition  | Waiver Potential | ACS                  |
|-------------------|------------|------------------|----------------------|
|                   |            | Waiver Authority | review/evaluation    |
| I/IA              | All stages | Maybe*+          | Maybe†               |
|                   |            | AETC             |                      |
| II/III            | All stages | Yes*#+           | Yes†                 |
|                   |            | AFMRA            |                      |
| ATC/GBO           | All stages | Yes*#+           | At the discretion of |
| SWA               |            | AFMRA            | the waiver authority |

<sup>\*</sup> FC I/IA candidates, as well as untrained FC II, FC III, GBO, ATC, and SWA; waiver may be considered five years after completion of treatment if asymptomatic and in full remission with a favorable prognosis. # For trained FC II, FC III, ATC/GBO, SWA individuals only, waiver may be considered six months after completion of treatment if asymptomatic and in full remission; the <a href="exception">exception</a> is for fighter aircrew who need to wait 12 months prior to waiver consideration if they received bleomycin, otherwise 6 months.

Review of AIMWTS in Apr 2015 revealed 31 members with a waiver request for the diagnosis of HL. There were two cases resulting in a disposition of disqualified. Breakdown of the cases was as follows: 13 FC II cases (0 disqualifications), 11 FC III cases (2 disqualifications), 5 ATC/GBC cases (0 disqualifications), and 2 MOD cases (0 disqualifications). One of the DQs was for recurrent disease and the other was due to side effects from treatment.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>+</sup> No indefinite waivers will be granted.

<sup>†</sup> For high performance (routine use of aviator mask while flying) individuals treated with bleomycin, <u>will no longer</u> require an ACS evaluation unless problems arise and the evaluation is requested by the waiver authority.

The AMS for <u>initial waiver</u> for Hodgkin lymphoma should include the following:

- A. History initial symptoms and signs, staging, treatment (amount and location of radiation and/or amount and type of chemotherapy), current symptoms/signs and activity level.
- B. Physical lymphoid regions, spleen and liver.
- C. Hematology/oncology reports to include all follow-up studies consistent with current guidelines in National Cancer Comprehensive Network (NCCN).
- D. CT scan results after treatment.
- E. Labs complete blood count (CBC), erythrocyte sedimentation rate (ESR), LDH, liver function tests, albumin, blood urea nitrogen (BUN), and creatinine.
- F. Submit ECG and echocardiogram (or MUGA scan) studies if the individual is treated with anthracycline containing regimens.
- G. Pulmonary function testing, with spirometry pre and post bronchodilator, lung volumes and DLCO. If there is any DLCO abnormality, exercise oximetry and/or metabolic exercise testing, and follow up DLCO in 3-6 months would be advisable to determine functional status and clinical course.
- H. Pathology report.
- I. Tumor board results (military or civilian).
- J. Medical evaluation board results.

The AMS for waiver renewal for Hodgkin lymphoma should include the following:

- A. History brief summary of stage with risk factors, treatment, review of symptoms for signs of recurrence or complications from treatment (include negatives), activity level.
- B. Physical thyroid, lung, cardiovascular, lymphoid regions, spleen and liver.
- C. Hematology/oncology consult.
- D. TSH if RT to mantle region.
- E. Labs CBC, platelets, ESR, and chemistry profile.

#### III. Overview.

HL (formerly Hodgkin's disease) is a neoplasm of lymphoid tissue that accounts for 12-30% of all malignant lymphomas. It has a bimodal distribution with a peak incidence between 15 and 30 years of age followed by another peak among adults over 55 years old and is more common among males. HL will be diagnosed in approximately 9,000 people in 2014 of which 1,180 will die. HL is divided into two main types by the World Health Organization classification: nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) and classical Hodgkin lymphoma (CHL). CHL is further divided into four subtypes: nodular sclerosis, mixed cellularity, lymphocyte-depleted, and lymphocyte-rich. CHL predominates in Western countries (95% of cases). The nodular sclerosis subtype of CHL is more common among young adults (15-35 years old) whereas NLPHL is more common during the fourth decade of life.

CHL is defined histopathologically by the presence of the malignant Reed-Sternberg cell in an inflammatory background of lymphocytes and fibrosis whereas NLPHL is characterized by the presence of lymphocyte-predominant cells (popcorn cells) distinguished by giant cells, which express typical B cell lineage.<sup>2</sup> Among CHL, nodular

sclerosis accounts for 50-80% of cases followed by mixed cellularity (20-30%), lymphocyte-rich (5%) and lymphocyte-depleted (<1%). 1-5

Common presenting features of CHL include painless lymphadenopathy (usually above the diaphragm), cough, fever, night sweats, and weight loss. The mediastinum is often involved. NLPHL most often presents with cervical or axillary lymphadenopathy and is distinguished from CHL in that mediastinal lymph nodes and extranodal organs are rarely involved.

Several large studies have demonstrated that a prior history of serologically confirmed infectious mononucleosis (in particular elevated titers of Epstein-Barr virus) confers about a three-fold increased risk for HL in young adults. Of note, EBV is implicated in 40% of CHL cases, most commonly the mixed cellularity subtype. An increased risk for HL among siblings and close relatives supports a genetic basis for increased susceptibility.

The extent of HL is classified using the four-stage modified Ann Arbor classification. Stage I is involvement of a single lymph node region (I) or extralymphatic site (I<sub>E</sub>). Stage II is involvement of two or more lymph node regions (II) or extralymphatic sites (II<sub>E</sub>) on the same side of the diaphragm. Stage III is involvement of lymph node regions on both sides of the diaphragm (III) or extralymphatic sites (III<sub>E</sub>) [Waldeyer's ring of lymphoid tissue in the oropharynx and the spleen both count as nodal sites]. Stage IV is diffuse or disseminated involvement of one or more extralymphatic organs or tissues. Extranodal/lymphatic sites primarily include bone marrow, liver, lungs and bones. The absence or presence of unfavorable factors such as fever, night sweats, and/or unexplained loss of 10% of more of body weight in the 6 months preceding diagnosis are denoted by the suffix letters A or B, respectively. The classic B symptoms are seen in ~25% and denote widespread or locally extensive disease. Fatigue and pruritus can also be seen in HL.<sup>2</sup>

The workup of HL should include a thorough history focusing on the presence or absence of B symptoms, alcohol intolerance, pruritus, and fatigue; a focused physical exam of the lymph nodes, spleen and liver; laboratory tests including a CBC with differential, platelets, ESR, LDH, albumin, LFT, renal function, chest x-ray, PET/CT and contrastenhanced CT. The preferred method for diagnosis is by excisional lymph node biopsy although core needle biopsy may be used. The role of fine-needle aspiration (FNA) is controversial and a negative FNA biopsy does not rule out lymphoma. The use of immunohistochemistry is also recommended.<sup>2</sup>

Prognosis varies depending primarily on stage of disease and histologic subtype, but Hodgkin lymphoma is now curable in 80% of cases as a result of improved management and treatment.<sup>2</sup> Nodular lymphocyte-predominate HL has the best prognosis, usually (80%) present as asymptomatic, limited stage disease. Nodular sclerosis usually carries a better prognosis than mixed cellularity, which in turn has a better prognosis than lymphocyte depletion.<sup>5</sup> With regards to prognosis and treatment, patients are classified into three groups: early-stage favorable (stage I-II with no unfavorable factors); early-stage unfavorable (stage I-II with any unfavorable factors); and advanced-stage disease

(stage III-IV).² The International Prognostic Factors Project Score (IPS) is used for risk stratification among patients with advanced-stage HL. This score was based on studies that found that patients with advanced-stage CHL (stage III-IV) experienced reduced survival rates 7-8% per year for each of the following factors: age greater than 45 years, male gender, stage IV disease, albumin <4 g/dL, Hgb < 10.5 g/dL, leukocytosis (>15,000/mm³), lymphocytopenia (<8% of WBC and/or count < 600/mm³).¹¹¹² Currently, the overall 5-year survival for HL is 81%.¹ B systemic symptoms, mediastinal mass to largest transthoracic diameter ratio >0.33 and extensive tumor burden (≥10 cm largest diameter of any single mass) are other factors that have been repeatedly documented as poor prognostic factors.²

Treatment for HL may involve radiotherapy, chemotherapy, or both, depending on the subtype (CHL vs. NLPHL), stage of disease, and the IPS score. For CHL, the ABVD (doxorubicin [Adriamycin®], bleomycin, vinblastine, and dacarbazine) and Stanford V (doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin and prednisone) protocols are most commonly used with involved field radiation therapy (RT). Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) can also be used.<sup>2</sup> PET/CT imaging is used for monitoring therapy and disease response. 1,2 For NLPHL, a combination of rituximab, multiagent chemotherapy, such as ABVD, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), or CVP (cyclophosphamide, vincristine, prednisone) plus involved field radiotherapy are used.<sup>1</sup> Stem cell transplantation and immunotherapy has been used in refractory HL with limited success. Monoclonal antibodies are currently in Phase II trials and FDA approved as second-line agents. Generally, individuals with limited-stage disease and nonbulky disease are treated with two cycles of ABVD followed by RT or four cycles of ABVD without RT. Individuals with advanced-stage disease (III-IV) or with B symptoms in any stage receive ABVD until two cycles beyond achieving complete remission. Individuals with bulky disease and in any stage receive ABVD plus RT. More recent studies have indicated that two cycles of ABVD followed by involved-field, moderate-dose radiation can cure most patients. 10

For early stage favorable HL (stage I-II), the 5 year failure rate for treatment (recurrent disease) is 9%.<sup>5</sup> For early stage unfavorable disease (stage I-II), the failure rate (relapse) is around 15%.<sup>5</sup> Relapse after successful treatment in advanced-stage occurs in 30% to 47% and most relapses occur within 4 years; about 10% of all relapses occur beyond 5 years.<sup>5</sup>

Although the likelihood of being "cured" of HL is high, overall expectation of survival is not normal. Long-term follow-up studies show that the cumulative treatment-related mortality rate exceeds that of HL itself in 15 years. The challenge is holding the potential for long-term toxicity to a minimum while successfully treating the disease initially. MOPP (mustargen, oncovin, procarbazine, and prednisone) is associated with infertility, premature menopause and/or leukemia/myelodysplasia. ABVD has less long-term toxicities and has proven therapeutic efficacy. Anthracyclines (e.g., doxorubicin) are associated with cardiomyopathy, bleomycin with pulmonary fibrosis, and alkylating agents with bone marrow failure. RT-induced second malignancies include non-HL,

breast, lung or gastrointestinal cancers. RT treatment to the neck area is associated with hypothyroidism and to the chest with cardiac disease. The practice of RT has improved; smaller fields, PET/CT imaging enhanced RT planning and intensity-modulated radiotherapy (IMRT) allows for better targeting and reduced radiation of uninvolved tissues. Fatigue is commonly reported in HL survivors. <sup>3, 11</sup>

Pregnancy, older age (>50 years old), and HIV infection can complicate care and treatment of HL. Among pregnant women, abdominal ultrasound can be used instead of CT/PET and treatment can sometimes be delayed until after delivery. Older patients with HL experience poorer treatment outcomes due to the toxic effects of treatment. They do, however, benefit from the use of doxorubicin. According to the literature, HIV patients should receive the same treatment as non-infected patients.<sup>12</sup>

#### IV. Aeromedical Concerns.

As with most malignancies, aeromedical health concerns of HL are based on the disease and the treatment. With HL, the risk for sudden incapacitation is minimal as disease involvement of the CNS or heart is rare. Although the most common presentation of HL is a superficial nontender mass, initial manifestations rarely may include hemoptysis (intrathoracic involvement) or neurologic symptoms from spinal cord compression. However, the greatest concern arises from the potentially rapid (weeks to months) degradation in mental and physical status when the HL and/or treatment protocol is aggressive. Damage to the cardiopulmonary, neurologic, endocrine, and reticuloendothelial systems may occur as a result of disease progression and/or radiotherapy/chemotherapy. In general, flyers can be returned to flight status once all therapy has been discontinued, adverse effects from therapy have resolved, and any hematologic deficits have normalized.<sup>13</sup>

In the past, the use of bleomycin in aviators would have been permanently disqualifying. This was based on the risk of pulmonary fibrosis with exposure to oxygen. The value of bleomycin in the treatment of malignancies is in part a function of its specific toxicity, since it does not induce bone marrow aplasia, and thus does not add to the toxicity that limits most oncologic drugs. Instead, the principal target organ of bleomycin-induced injury is the lung, with acute pulmonary damage occurring in 6-18% of treated patients. The pathophysiology of delayed toxicity of bleomycin is complex. In the medical literature of the last thirty years, a number of patients have been described who, having previously received bleomycin therapy; have developed pulmonary toxicity when undergoing subsequent surgery. Typically, these have been young individuals receiving modest levels of oxygen (33-42%) during long operations (4-8 hours). The true incidence of such delayed toxicity is unknown, since the subsequent literature has largely consisted of isolated case reports or small series.<sup>14</sup> A more cogent argument can be made that the period of risk is primarily in the first year after therapy, since most cases occurred within that time frame. However, it is equally possible that this observation represents a bias related to the timing of operative intervention.

Applicable data had been non-existent, a state of affairs that has been somewhat altered by unpublished data recently supplied by the Duke Hyperbaric Unit.<sup>14</sup> Although it had been the practice in hyperbaric medicine to avoid hyperoxia in bleomycin-treated individuals, the undoubted benefit from hyperbaric oxygen (HBO) in wound healing and osteonecrosis posed against the uncertain risk of delayed bleomycin toxicity led several years ago to a change in policy. Since then, the Duke unit has treated 11 individuals previously exposed to bleomycin with HBO. There was a wide range of time between the last dose of bleomycin and the institution of HBO, ranging from 1 month to 22 years. The range of cumulative bleomycin doses was not noted. Anywhere from 8 to 44 treatments with 100% oxygen at 2 ATA (PiO2 ~ 1475 mmHg) were administered for two hours per treatment, once or twice daily. One individual experienced significant chest discomfort and a decline in diffusion capacity of 50%; both resolved following a break in treatment, and she successfully completed HBO treatment with a reduction in frequency of her sessions. While the Duke experience does not represent occupational exposure per se, and the number of individuals treated is small, the amount of oxygen exposure from HBO therapy is far in excess of what would be expected in aviation, and suggests that the risk of delayed toxicity outside the operating room may be minimal.

Based on this data, policy was changed for aviators treated with bleomycin. Those aviators returning to non-high performance aircraft would be evaluated as usual, addressing risks of tumor recurrence and potential toxicity from chemotherapy. Assuming they had not developed bleomycin pneumonitis during therapy, then no restrictions from altitude chamber or other sporadic oxygen exposure is warranted. Because it is possible, and biologically plausible, that the common perception of an increased period of risk within the first year is correct, a grounding period of one year from the end of treatment is required before waiver consideration in high performance aircrew. In most cases, this will coincide with the grounding period already recommended as a result of the disease/chemotherapeutic regimen.

There have been case reports of life-threatening pneumonitis developing in patients with a history of bleomycin-induced lung injury, who were later given supplemental oxygen for surgical procedures. Therefore, aviators who have a history of bleomycin-induced lung injury should not be allowed to return to airframes that require routine use of 100% oxygen. Also, they should be exempted from the portions of the altitude chamber qualification that require 100% oxygen use. Use of 100% oxygen during emergencies such as fire or rapid decompression is acceptable and should not be discouraged.

Aviators treated with anthracyclines (e.g. doxorubicin) are at risk of treatment-induced cardiomyopathy. The aeromedical risk due to poor left ventricular function as a result of anthracycline containing treatment regimens requires demonstration of adequate cardiac function. An echocardiogram or Multi-Gated Acquisition (MUGA) scan may be required to demonstrate adequate cardiac function for consideration of returning an aviator to flying following treatment with anthracyclines.

| ICD-9 Codes for Hodgkin lymphoma |   |  |
|----------------------------------|---|--|
| 201.4                            | Hodgkin's disease, lymphocytic-histiocytic predominance |  |
| 201.5                            | Hodgkin's disease, nodular sclerosis                    |  |
| 201.6                            | Hodgkin's disease, mixed cellularity                    |  |
| 201.7                            | Hodgkin's disease, lymphocytic-depletion                |  |
| 201.9                            | Hodgkin's disease (lymphoma), unspecified               |  |

| ICD-10 Codes for Hodgkin lymphoma |   |  |
|-----------------------------------|---|--|
| C81.00                            | Nodular lymphocyte predominant Hodgkin lymphoma, unspecified site |  |
| C81.10                            | Nodular sclerosis classical Hodgkin lymphoma, unspecified site    |  |
| C81.20                            | Mixed cellularity classical Hodgkin lymphoma, unspecified site    |  |
| C81.30                            | Lymphocytic-depleted classical Hodgkin lymphoma, unspecified site |  |
| C81.90                            | Hodgkin's lymphoma, unspecified, unspecified site                 |  |

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### WAIVER GUIDE

Updated: May 2015

Supersedes Waiver Guide of Jan 2013

By: Maj Amy Gammill (Chief ACS Internal Medicine branch) and Dr Dan Van Syoc

#### **CONDITION:**

**Human Immunodeficiency Virus (HIV) Infection (May 2015)** 

#### I. Waiver Consideration.

Human immunodeficiency virus (HIV) infection is disqualifying for all flying class personnel per Air Force policy. Primarily because of the risk neurocognitive impairment even in the early stages of disease, aeromedical waiver is not recommended for this condition. ATC, GBO and SWA personnel are also disqualified for retention duties so will require an AMS for disposition from their special duty assignments.

**Table 1: Waiver potential for HIV infections** 

| Flying Class  | Condition      | Waiver Authority | ACS               |
|---------------|----------------|------------------|-------------------|
|               |                |                  | Review/Evaluation |
| I/IA          | HIV positivity | AETC             | No                |
| II/III        | HIV positivity | AFMRA            | If requested by   |
|               |                |                  | waiver authority  |
| ATC, GBO, SWA | HIV positivity | AFMRA            | If requested by   |
|               |                |                  | waiver authority  |

AIMWTS search in Mar 2015 produced 41 cases with the diagnosis of HIV infection. All were disqualified. There were no FC I/IA cases, 14 FC II cases, 20 FC III cases, 6 ATC/GBC cases, and 1 MOD case. One of the earlier FC III cases was originally given a waiver and then disqualified less than one year later due to a decreased CD4 count.

## II. Information Required for Waiver Submission.

Active duty Air Force members and Air Reserve Component (ARC) members on extended duty are referred to San Antonio Military Medical Center (SAMMC) for initial medical evaluation and medical evaluation board (MEB) to determine fitness for duty. ARC members not on extended active duty must obtain a medical evaluation that meets the requirements of Attachment 8 in AFI 44-178, *Human Immunodeficiency Virus Program*, from their civilian healthcare provider (in the case of the Air National Guard (ANG), only if the state identifies a nonmobility, nondeployable position in which the member can be retained). The immediate commander of ARC members not on extended active duty will determine if the member can be utilized in the Selected Reserve.

Information required for a waiver for HIV should include:

- A. All pertinent medical history and laboratory data.
- B. Reports from all treating physicians, particularly infectious disease providers.
- C. If not already accomplished, an MEB is mandatory for continued military service.

If there is a request for the ACS to review the case, the following are required:

- A. All Infectious Disease Consultant notes.
- B. CD 4 counts at diagnosis and on therapy.
- C. Viral loads (viral RNA levels) at diagnosis and on therapy.
- D. Complete metabolic panel and CBC at baseline and on therapy.
- E. Description of drug regimen (including duration, compliance and side effects).
- F. Lipid panel and fasting glucose or HbA1C on therapy.
- G. Continued surveillance plan.

#### III. Overview.

HIV is a retrovirus that likely evolved from simian immunodeficiency virus in chimpanzees, perhaps as early as 1968. The syndrome of acquired immunodeficiency syndrome (AIDS) was first described in 1981 as a severe form of immune deficiency in homosexual men. At that time, the disease appears to have been confined for the most part to Africa, the Caribbean, and North America, but over the next two decades the disease reached epidemic proportions throughout the world. The disease is predominantly transmitted via sexual contact, intravenous access (illicit drug use and transfusions), and transplacental in the perinatal period; currently, about 80% of transmission worldwide is believed to occur via heterosexual intercourse. With the introduction of combination antiretroviral therapy (cART), the natural history of the disease has changed, with long-term survival proving to be relatively common; cART is not curative, however, and therapy is lifelong.<sup>1</sup>

Infection with HIV is commonly asymptomatic in its early stages, with the presence of early symptoms correlating with more rapid progression to AIDS.<sup>2</sup> The infection at this point is diagnosable by measuring viral RNA copies. Seroconversion, with the development of specific antibodies detectable on standard ELISA testing, occurs within weeks to months, with over 95% converting within six months.<sup>3</sup> A small percentage (7% in one study) of individuals are able to spontaneously control their viremia.<sup>4</sup> For the first six months after transmission, the disease is usually latent, with no findings except occasional lymphadenopathy. Lymphoid tissue is the primary reservoir of infection. Helper T lymphocytes (cluster determinant 4, or CD4) are predominantly affected, with remarkable turnover of both virus and CD4 cells in the early stages of disease. In the great majority of patients, CD4 levels eventually decline from their pre-morbid value of ~1,000/mm<sup>3</sup>, with the CD4 count correlating well with risk of infection. After the first year, CD4 counts drop an average of 50/mm<sup>3</sup> annually. Staging is largely by CD4 counts, and is depicted in Table I. AIDS is defined by a CD4 count of 200/mm<sup>3</sup> or by an AIDSdefining complication; about 10% of patients develop the latter while their CD4 count is still above 200/mm<sup>3</sup>. HAART is now recommended for all HIV-positive patients

according to Department of Health and Human Services HIV treatment guidelines and the 2014 International Antiviral Society-USA Panel.<sup>6,7</sup>

**Table 2 – AIDS Surveillance Case Definitions**<sup>26</sup>

| CD4 cell                     | A – Asymptomatic,             | B – Symptomatic | C – AIDS indicator |
|------------------------------|-------------------------------|-----------------|--------------------|
| categories                   | PGL <sup>#</sup> or acute HIV | (not A or C)*   | condition          |
|                              | infection                     |                 |                    |
| $>500/\text{mm}^3 (\ge 29$   | A1                            | B1              | C1                 |
| percent)                     |                               |                 |                    |
| 200-499/mm <sup>3</sup> (14- | A2                            | B2              | C2                 |
| 28 percent)                  |                               |                 |                    |
| <200/mm <sup>3</sup> (<14    | A3                            | B3              | C3                 |
| percent)                     |                               |                 |                    |

1993 AIDS surveillance case definition for adolescents and adults. All patients in categories A3, B3, C1-C3 are reported as AIDS based upon prior AIDS-indicator conditions and/or a CD4 cell count <200/mm³. AIDS-indicator conditions include three new entities added to the 1987 case definition: recurrent bacterial pneumonia, invasive cervical cancer, and pulmonary tuberculosis.

CD4 count correlates less well with other complications, including neurologic involvement. Encephalitis from AIDS was initially thought to be due to opportunistic organisms such as cytomegalovirus.<sup>8</sup> It soon became clear, however, that HIV itself was responsible. Invasion of the central nervous system commonly occurs early in the course of disease, as soon as 16 days after transmission. 10 The virus probably gains access to the central nervous system (CNS) through infected macrophages, a route known as the Trojan Horse mechanism. 11 Once in the brain, the virus targets the glia, the supporting cells that represent 90% of brain cells. There is little evidence that neurons themselves are infected, though the involvement of surrounding cells eventually leads to neuronal death. From post-mortem studies, the virus appears to have a predilection for subcortical white matter and the basal ganglia. About half to two-thirds of patients with HIV develop clinical neurologic disorders.<sup>12</sup> Though the introduction of HAART has been associated with a decrease in the incidence of frank dementia, the prevalence of HIV encephalopathy has actually risen over the same period. 13 This suggests that while antiretroviral therapy reduces some of the severe neural manifestations, such therapy has had little effect on the virus's involvement of the CNS. Therefore, HIV infection of the CNS presents a serious barrier to the management and eradication of the virus.<sup>14</sup>

New onset seizures occur in 2-8% of HIV patients; about half of these are due to infectious complications or comorbid conditions, while the remaining half appear to be directly due to HIV itself.<sup>15</sup> Psychiatric manifestations are common, likely due to a combination of demoralization, social isolation, and chronic stress, as well as direct CNS

<sup>#</sup> Persistent Generalized Lymphadenopathy

<sup>\*</sup>Symptomatic conditions not included in category C that (a) are attributable to HIV infection or indicate a defect in cell-mediated immunity or (b) are conditions considered to have a clinical course or to require management that is complicated by HIV infection. Examples of B conditions include but are not limited to bacillary angiomatoses; thrush; vulvovaginal candidiasis that is persistent, frequent or poorly responsive to therapy; cervical dysplasia (moderate or severe); cervical carcinoma in situ; constitutional symptoms such as fever (38.5°C) or diarrhea for more than one month; oral hairy leukoplakia; and herpes zoster involving two episodes or more than one dermatome.

involvement. Major depression affects 15-40% of patients with HIV, a rate that is far in excess of the general population. Although some of the populations most affected by HIV may be at increased risk of depression, meta-analysis of ten published studies comparing HIV-positive individuals to at-risk HIV-negative controls found a two-fold increase in prevalence of major depression with the former group. Unlike depression, AIDS mania is a complication of late-stage disease, and has diminished in frequency with the introduction of HAART.

Although the conditions described in the previous paragraph have the potential for severe morbidity, the most common neurologic complications are neurocognitive disorders. Major or mild neurocognitive disorder due to HIV infection occurs in up to 25% of individuals with HIV infection. The earliest reports of CNS disease described cases of frank dementia. HIV-associated dementia (HAD) is a subcortical process, characterized in its early stages by impaired attention-concentration, abnormal memory, mental and motor slowing, and incoordination. As is typical for a subcortical dementia, language is generally spared. By definition, HAD entails moderate-to-severe cognitive impairment, and marked difficulty in carrying out activities of daily living (ADL). A milder form of the same disorder was also identified and labeled as minor cognitive-motor disorder (MCMD); characteristics were similar to HAD, but with mild-to-moderate cognitive impairment, and mild interference with ADL (e.g., difficulty managing finances, problems with medication schedules). The criteria for these two disorders were described by an American Academy of Neurology Task Force in 1991. However, a number of reports began appearing over the ensuing decade which described subclinical neurocognitive abnormalities in association with HIV infection; these abnormalities involved similar cognitive functions, and were apparent on testing but were not grossly evident to the patient or to companions. 19-21 Some studies, in contrast, were unable to document similar abnormalities.<sup>22, 23</sup> A review of available research found that identification of such abnormalities was largely determined by the nature of the cognitive test battery, with abbreviated exams usually failing to demonstrate the deficiencies.<sup>24</sup>

In 2007, the National Institute of Mental Health and the National Institute of Neurologic Diseases and Stroke convened a working group to evaluate the validity of these findings, and to refine the definitional criteria. The group adopted the collective term HIV-associated neurocognitive disorders (HAND), and recognized three subcategories, consisting of HAD, mild neurocognitive disorder (MND, similar to MCMD), and asymptomatic neurocognitive impairment (ANI). Neurocognitive impairment of any of these three categories was noted to be prevalent throughout all HIV stages, with 27% of CDC stage A, 44% of stage B, and 52% of stage C affected (see Table 1). Epidemiologic data from the post-HAART era showed that, as the disease progressed through the stages, the prevalence of ANI slowly decreased, the prevalence of MND markedly rose, and HAD prevalence remained under 5%. One issue noted from multiple studies was the instability of HAND, with about 20% of individuals showing fluctuating mental status from one examination to another. (Such fluctuation is not unique to HIV; it is particularly characteristic, for instance, of the dementia that may complicate multiple sclerosis).

#### IV. Aeromedical Concerns.

Aviation is a demanding discipline, requiring a high degree of cognitive capability in an occupation with significant inherent risk. Clearly any mental disorder that impairs ADL is incompatible with aviation. In addition, measurable neurocognitive abnormalities, even if not severe enough to impair routine activities, are considered to be potentially significant for aviation. Furthermore, certain conditions encountered in flying, particularly reduced ambient oxygen pressure, would be expected to unmask an underlying cognitive deficiency. It is notable that in one of the early reviews of HIV encephalopathy, the authors noted that of those patients whose dementia appeared suddenly, approximately half did so under the stress of hypoxia.<sup>27</sup> Thus cognitive function would be at greatest risk under actual aviation conditions. There is also a risk of depression and suicide (relative rate 20 as compared to USAF controls) during the adjustment reaction phase. Other potential aeromedical concerns include the aviator's emotional reaction to the diagnosis of HIV, side effects of treatment regimens, and the need for close observation of the patient.<sup>28</sup> While most first-line agents for HIV management are relatively well-tolerated in comparison to older regimens, the range of therapeutic options is broad, with six classes of medications and over 20 drugs currently available. Therefore risk of toxicity and intensity of monitoring for medication side effects must be considered on a case-by-case basis.

Qualification for worldwide military duty must be considered for any HIV-seropositive individuals. In fact, issues of worldwide deployment to areas of limited medical resources, use of attenuated live virus vaccines, and the use of the military as its own walking blood bank were all reasons cited for mandatory HIV testing of military personnel beginning in 1985.

| ICD-9 code for HIV |                                      |
|--------------------|--------------------------------------|
| 042                | Human Immunodeficiency Virus Disease |

| ICD-10 code for HIV |  |  |
|---------------------|--|--|
| B20                 | Human Immunodeficiency Virus (HIV) Disease |  |

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## Hypercholesterolemia (Feb 2019)

Authors/Reviewers: Dr. Christopher Keirns, Maj Laura Bridge, and Capt Luke Menner (ACS Internal Medicine); and Dr. Dan Van Syoc (Deputy Chief, ACS).

**Significant Changes:** Waiver guide updated to reflect the 2018 guideline on the management of blood cholesterol from the American Heart Association/American College of Cardiology (AHA/ACC) and others.

## I. Waiver Consideration

Hypercholesterolemia that is treated with monotherapy using one of the aeromedically-approved lipid-lowering agents is not disqualifying. The use of more than one lipid-altering medication or the use of any aeromedically-unapproved medication is disqualifying for flying classes I/IA, II, and III. For ground-based and other special duty operators, combination therapy is not disqualifying, but the use of any aeromedically-unapproved medications is disqualifying. Factors that are considered when assessing suitability for waiver include whether the treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the risks associated with the specific medication(s), the individual service member's tolerance of the medication(s), adherence to therapy, and the cumulative risk of all co-morbid conditions (e.g., diabetes mellitus, heart disease, etc.).

Waiver requirements follow the recommendations established in the "2018 AHA/ACC Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology / American Heart Association Task Force on Clinical Practice Guidelines." Individuals who meet criteria for cholesterol treatment but are not on an appropriate regimen will not be considered waiver-eligible. Waiver can be considered once an aviator is tolerating a stable medication regimen without adverse effects.

Table 1: Waiver potential for hypercholesterolemia

| Flying Class (FC) | Condition   | Waiver Authority<br>Waiver Potential | ACS Review or Evaluation |
|-------------------|---|--------------------------------------|--------------------------|
| I/IA              | Hypercholesterolemia treated<br>with medication other than a<br>single aeromedically-<br>approved agent           | Yes<br>AETC                          | Yes                      |
|                   | Repeat fasting LDL > 190 mg/dL, with or without risk factors; or > 160 mg/dL with at least 2 cardiac risk factors | Yes<br>AETC                          | Yes                      |
| II/III            | Hypercholesterolemia<br>requiring use of a medication<br>other than a single<br>aeromedically-approved<br>agent   | Yes<br>MAJCOM <sup>1</sup>           | No                       |
| GBO/ATC/SWA       | Not Disqualifying <sup>1,2</sup>  | N/A                                  | N/A                      |

<sup>1.</sup> Use of any medication that is not included on the approved-medication list is disqualifying, and the waiver authority is AFMRA.

## I. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. List all risk factors for atherosclerotic cardiovascular disease (ASCVD)
    - i. Non-modifiable risk factors (age, gender, race/ethnicity, family history)
    - Modifiable risk factors (tobacco use, current blood pressure, personal history of diabetes, personal history of treatment for hypertension)
  - b. List all treatments trialed, their effectiveness, and any adverse effects
  - c. List current medications, doses, and adverse effects
  - d. List all co-morbid conditions and describe degree of control
- 2. Laboratory studies required:
  - a. Baseline fasting lipid panel before starting treatment
  - b. Baseline fasting comprehensive metabolic panel (CMP)
- 3. Current physical examination findings.
- 4. Any other pertinent information.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

<sup>2.</sup> Hypercholesterolemia is NOT disqualifying for GBO, ATC, or Special Warfare duties if all medications being utilized are included on the applicable career field approved medication list.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Any changes in ASCVD risk factors
  - b. Current medications, doses, and adverse effects
  - c. Updated fasting lipid panel
  - d. Updated fasting CMP
- 2 Current physical examination findings.
- 3 Any other pertinent information.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## **III. Aeromedical Concerns**

While hypercholesterolemia is typically asymptomatic, it is a common and treatable risk factor in the development of ASCVD. The manifestations of ASCVD, which include coronary heart disease (myocardial infarction, angina, heart failure, and sudden cardiac death), cerebrovascular accident (stroke and transient ischemic attack), aortic atherosclerotic disease and aneurysm, and peripheral artery disease, can be potentially catastrophic, resulting in sudden incapacitation in the aviation environment. Additionally, these diseases are individually disqualifying for continued aviation duties and may not be eligible for waiver, depending upon crew position, disease severity, required therapies, and a variety of other factors. Furthermore, very high triglyceride levels may result in acute pancreatitis, which can be suddenly incapacitating (please refer to the "Pancreatitis" Waiver Guide for specific information about this diagnosis). Due to the risks associated with these outcomes, it is of critical importance to intervene early to reduce the possibility of an event that could result in devastating consequences for both the health of the affected service member and the success of the aviation mission.

Review of AIMWTS data in Jan 2019 revealed 260 members with an AMS containing the diagnosis of hyperlipidemia since Jan 2014. Of that total, 2 were FC I/IA (1 disqualified), 102 were FC II (5 disqualified), 7 were RPA pilots (1 disqualified), 71 were FC III (11 disqualified), 10 were ATC/GBC (1 disqualified), and 0 were MOD. Review of the cases revealed that these disqualifications resulted from other active co-morbid conditions.

| ICD-9 codes for hyperlipidemia |                           |
|--------------------------------|---------------------------|
| 272.0                          | Pure hypercholesterolemia |
| 272.1                          | Pure hyperglyceridemia    |
| 272.2 Mixed hyperlipidemia     |                           |

| ICD-10 codes for hyperlipidemia |                           |
|---------------------------------|---------------------------|
| E78.0                           | Pure hypercholesterolemia |
| E78.1                           | Pure hyperglyceridemia    |
| E78.2                           | Mixed hyperlipidemia      |

## **IV. Suggested Readings**

- Grundy SM, Stone NJ, Bailey AL, et al. 2018
   AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA
   Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018; Available at <a href="http://www.onlinejacc.org/guidelines/cholesterol">http://www.onlinejacc.org/guidelines/cholesterol</a>
- 2. ACC ASCVD Risk Estimator Plus. Available at <a href="https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/">https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/</a>
- 3. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract 2017; 23(Suppl 2):1-87. Available at <a href="https://www.aace.com/files/lipid-guidelines.pdf">https://www.aace.com/files/lipid-guidelines.pdf</a>

#### WAIVER GUIDE

Updated: Jan 2014

Supersedes Waiver Guide of Jul 2010

By: Capt Dan Pizzino (RAM XV), Maj Chris Keirns (ACS Internal Medicine), and Dr Dan

Van Syoc

## **CONDITION:**

Hypertension (Jan 2014)

## I. Waiver Consideration.

Hypertension that is not controlled with a single approved agent or with lifestyle changes is disqualifying for FC I/IA, FC II, FC III, and ATC/GBC personnel. Aviators with hypertension responsive to lifestyle modifications should have serial BP rechecks quarterly to semi-annually during the first year to assure success of the lifestyle modifications. Failure to achieve blood pressure control with lifestyle modifications, or an initial blood pressure average exceeding 160 mmHg systolic or 100 mmHg diastolic, requires initiation of pharmacotherapy. The rated or non-rated aviator (to include ATC/GBO personnel) with a history of isolated HTN who remains normotensive using lifestyle modifications or one of the following approved medications as monotherapy (thiazide, with or without triamterene, ACEi [lisinopril or ramipril], or ARB [losartan or telmisartan]) does not require a waiver. The aviator requires a minimum of seven days grounding after initiation of pharmacotherapy. Their BP should be controlled below 140/90 mmHg (or below 150/90 mm Hg if 60 years of age or older), and they should be free of medication side effects prior to return to full duty; this includes all subsequent dose adjustments. For retention purposes, hypertensive cardiovascular disease is disqualifying for all classes to include ATC/GBO/SWA personnel.

Table 1. Anti-hypertensive medications and the waiver authority for specific flying classes.

| Flying<br>Class | Medications   | Waiver Potential<br>Waiver Authority | Duration      |
|-----------------|---|--------------------------------------|---------------|
| I, IA           | HTN, if controlled with a thiazide <sup>1</sup> (HCTZ or chlorothiazide), lisinopril, ramipril <sup>2</sup> , losartan or telmisartan   | Waiver not required                  | N/A           |
|                 | HTN, if controlled on other medication than listed above and/or in combination.   | No<br>AETC                           |               |
| II              | HTN, if controlled with a thiazide <sup>1</sup> (HCTZ or chlorothiazide), lisinopril, ramipril <sup>2</sup> , losartan or telmisartan   | Waiver not required                  | N/A           |
|                 | HTN, if controlled on HCTZ combined with lisinopril, ramipril <sup>2</sup> , losartan or telmisartan; atenolol <sup>3</sup> alone or in combination; nifedipine (coat-core or GITS) alone or in combination; or amlodipine alone or in combination  | Yes <sup>4, 5</sup><br>AFMRA         | Up to 3 years |
| III/ATC         | HTN, if controlled with a thiazide <sup>1</sup> (HCTZ or chlorothiazide), lisinopril, ramipril <sup>2</sup> , losartan or telmisartan   | Waiver not required                  | N/A           |
|                 | HTN, if controlled on HCTZ combined with lisinopril, ramipril <sup>2</sup> , losartan or telmisartan; atenolol <sup>3</sup> alone or in combination; nifedipine (coat-core or GITS) alone or in combination; or amlodipine alone or in combination  | Yes <sup>5</sup><br>MAJCOM           | Up to 3 years |
| ATC/GBO         | HTN, if controlled on medical therapy including combination therapy. Waiver required only if evidence of end organ damage.  | Waiver not required                  | N/A           |
|                 | HTN with associated end organ damage (outlined below); controlled on HCTZ combined with lisinopril, ramipril <sup>2</sup> , losartan or telmisartan; atenolol <sup>3</sup> alone or in combination; nifedipine (coat-core or GITS) alone or in combination; or amlodipine alone or in combination | Yes<br>MAJCOM                        | Up to 3 years |

Note: Uncontrolled hypertension is disqualifying for all aircrew, wavier eligible only if controlled.

<sup>1</sup> With or without triamterene. If potassium is added, a waiver will be required.

<sup>2</sup> Ramipril restricted to dosages of 5 mg to 20 mg.

<sup>3</sup> Third line drug, used after all others failed or were not tolerable. For aviators not required to fly in high-G aircraft.

<sup>4.</sup> FC II aviators on these medications can be waived, but only for FC IIA.

<sup>5.</sup> Waiver authority for initial FC II and FC III is AETC

An AIMWTS search in Nov 2013 produced a total of 877 current waiver submissions for the diagnosis of hypertension. Breakdown of these waivers revealed 9 FC I/IA cases (2 disqualifications), 387 FC II cases (28 disqualifications), 398 FC III cases (41 disqualifications), 74 ATC/GBC cases (9 disqualifications), and 9 MOD cases (2 disqualifications).

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. Waiver is required for hypertension only if pharmacotherapy involves more than one medication (with the exception of HCTZ and triamterene) or the use of one of the following (alone or in combination with another approved medication): atenolol, amlodipine, and nifedipine.

The AMS for the <u>initial waiver</u> for essential hypertension should include the following: A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.

- B. History summary of blood pressures, risk factors/co-morbidities including negatives [diet (especially, alcohol and sodium intake), botanicals/supplements, cigarette smoking/tobacco use, physical activity level, family history of premature cardiovascular disease, dyslipidemia, diabetes mellitus, sleep apnea (snoring, observed apneas)], symptoms including negatives (flushing, headaches, nocturia, chest pain, and claudication), previous treatments, medications and side effects.
- C. Physical weight (BMI), fundus for hypertensive retinal changes, thyroid, heart, lungs, auscultation for carotid, abdominal, and femoral bruits, abdominal exam for enlarged kidneys, masses, and abnormal aortic pulsation, lower extremity exam for edema and pulses and neurological assessment.
- D. Labs hematocrit/hemoglobin, fasting glucose, serum electrolytes, serum calcium, blood urea nitrogen (BUN), serum creatinine (Cr), lipid profile, thyroid stimulating hormone (TSH), and urinalysis.
- E. Resting electrocardiogram (ECG).
- F. 3-day blood pressure check demonstrating BP stable at goal at least one week after medication initiated.

The AMS for <u>waiver renewal</u> for essential hypertension should include the following: A. Interval history - summary of the intervening blood pressure control, symptoms related to coronary artery disease or medications, diet (e.g., alcohol and sodium intake) and supplements, cigarette smoking/tobacco use, physical activity level, other co-morbid medical conditions since last waiver granted.

- B. Physical blood pressure readings over the course of the previous waiver, weight changes, hypertensive retinal changes, auscultation for carotid, abdominal, and femoral bruits, heart and lungs, abdominal exam for enlarged kidneys, masses, and abnormal aortic pulsation, lower extremity exam for edema and pulses, and neurological assessment.
- C. Labs for all medications a renal panel (to include Cr and potassium) annually.
- D. 3-day blood pressure check.

#### III. Overview.

Hypertension (HTN) affects more than 70 million Americans. The complications caused by HTN, are the leading cause of death worldwide, and HTN remains the most frequent cause of outpatient clinic visits. Hypertension is also the easiest to treat risk factor of stroke, MI and heart failure, kidney disease, and peripheral vascular disease. The relationship between blood pressure (BP) and risk of cardiovascular disease (CVD) events is continuous, consistent, and independent of other risk factors. The higher the BP, the greater is the chance of myocardial infarctions, heart failure, stroke, and kidney disease. For individuals 40–70 years of age, each increment of 20 mmHg in systolic BP (SBP) or 10 mmHg in diastolic BP (DBP) doubles the risk of CVD across the entire BP range from 115/75 to 185/115 mmHg.

The 7<sup>th</sup> Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classification of hypertension, based on two or more properly measured readings, with confirmation of an elevated reading in the contralateral arm, at each of two or more visits after an initial screen, is listed in Table 1. These definitions did not change with JNC 8, published ahead of print in December 2013.

Table 2. Blood Pressure Classification.<sup>1</sup>

| Condition                  | SBP (mmHg)       | DBP (mmHg)           |
|----------------------------|------------------|----------------------|
| Normal BP                  | <120             | and <80              |
| Pre-hypertension (Pre-HTN) | 120-139          | or 80-89             |
| HTN  • Stage 1  • Stage 2  | 140-159<br>≥ 160 | or 90-99<br>or ≥ 100 |

<sup>&</sup>lt;sup>1</sup>These definitions apply to adults on no antihypertensive medications and who are not acutely ill. If disparity exists in categories between SBP and DBP, the higher value defines the severity of the HTN.

For aeromedical purposes, the USAF defines hypertension for flying personnel as a 3-day average systolic blood pressure greater than 140mm Hg or a 3-day average diastolic blood pressure greater than 90mm Hg. Asymptomatic trained flying personnel with average systolic blood pressure ranging between 140 mmHg and 160 mmHg, or average diastolic blood pressure ranging between 91 mmHg and 100 mmHg, may remain on flying status for up to 6 months (from the date the elevated blood pressure was first identified) while undergoing non-pharmacological intervention to achieve acceptable values.

While HTN is the dominant risk factor for stroke, coronary disease is associated with a number of other risk factors that are often co-morbid with HTN, and should be addressed at the same time. These include obesity, dyslipidemia, diabetes, cigarette smoking, and physical inactivity. Additional but non-modifiable risk factors for CVD include a family history of premature CVD and the patient's age.

Identifiable causes of HTN should be considered in all patients, especially when HTN is initially diagnosed under the age of 30 in a non-obese individual with no family history,

when the onset of HTN is rapid or severe, or when a patient's HTN does not respond to treatment. Although most HTN is idiopathic, relatively common causes of secondary hypertension include alcohol use, obesity, sleep apnea, and renal disease. These are readily addressed by history, physical exam, or initial lab studies. Pursuing a work-up for rarer causes of secondary HTN (e.g., renal vascular disease) should be guided by consultation with an internist or nephrologist.

Lifestyle modifications, which are listed in Table 2, are often effective at treating HTN and are associated with improvement in a patient's other major CVD risk factors and should always be considered as first-line treatment. If lifestyle modifications alone are inadequate, medical therapy is indicated. JNC 8 broadened the recommendations regarding initial choice of antihypertensive but still recommends thiazide-type diuretics for most patients without compelling indication for another antihypertensive medication class.

**Table 3. JNC-8 Recommendations** 

| Modification   | Recommendation  | Approximate SBP<br>Reduction (Range) |
|--|---|--------------------------------------|
| Weight reduction (10kg/22lbs)  | Maintain normal body weight (body mass index 18.5–24.9 kg/m2)   | 5–20 mmHg                            |
| Adopt Dietary Approaches<br>to Stop Hypertension<br>(DASH) eating plan | Consume a diet rich in fruits, vegetables, and low fat dairy products with a reduced saturated fat and total fat content.   | 8–14 mmHg                            |
| Dietary sodium reduction   | Reduce dietary sodium intake<br>to no more than 100 mmol/day<br>(2.4g sodium or 6g sodium<br>chloride)  | 2–8 mmHg                             |
| Physical activity  | Engage in regular aerobic physical activity (at least 30 min per day, most days of the week)  | 4–9 mmHg                             |
| Moderation of alcohol consumption                                      | Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons. | 2–4 mmHg                             |

In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence of approximately 35–40%; myocardial infarction, 20–25%; and heart failure, more than 50%. The Framingham Heart Study confirmed the benefit of long-term

antihypertensive therapy on CVD disease incidence and mortality with a 40% reduction of a 10-year risk of CVD death for treated versus untreated HTN. For aeromedical purposes the goal of antihypertensive therapy in patients under age 60 with uncomplicated HTN is to reach a BP below 140/90 mmHg. In accordance with JNC 8, the goal BP in patients 60 years of age or older with uncomplicated HTN is now less than 150/90 mmHg.

## IV. Aeromedical Concerns.

It should be noted that hypertension is almost never a risk factor for sudden incapacitation, particularly if it is controlled. However, the secondary complications of hypertension are of aeromedical significance. There is increased risk of end organ damage with long standing hypertension and includes hypertension associated with any of the following: More than minimal demonstrable changes in the brain. Heart disease related to the hypertension, including atrial fibrillation, moderate to severe left ventricular hypertrophy, and symptomatic systolic or diastolic dysfunction, impairment of renal function and grade III (Keith-Wagener-Parker) changes in the fundi. Furthermore, multiple drug therapy can require inordinate amount of medical supervision to include frequent blood pressure checks and recurrent laboratory monitoring making flight duties difficult. The longer term vascular complications of HTN are an increased risk of cardiovascular events such as myocardial infarction and stroke, potentially resulting in sudden incapacitation, or death. Because lifestyle modifications are considered to be first line interventions and are associated with negligible aeromedical side effects, each aviator should be individually evaluated for potential benefit from lifestyle modifications, used alone or in combination with medication(s). While numerous medications are effective in lowering BP, some drugs have modes of action that may adversely affect the flyer. Medications that act via direct vasodilatation or autonomic vasoregulation are avoided in favor of those that work via volume reduction, such as diuretics, or via the renin-angiotensin axis, such as angiotensin converting enzyme inhibitors (ACEi), or angiotensin receptor blockers (ARB). Medications that affect cognitive capacity (e.g., central  $\alpha$ -adrenergic agonists) should also be avoided.

The classes of antihypertensive agents available to USAF aviators include diuretics (thiazide, with or without triamterene), ACEi (lisinopril or ramipril) and ARB (losartan or telmisartan). These drugs are effective as monotherapy and when used as such do not require a waiver as long as the blood pressure is controlled and there are no adverse affects from the medication. All other medications will require a waiver. If those aviators on diuretics require potassium supplementation, they will require a waiver or they should be switched to a medication that does not require potassium replacement. The combination of diuretic with ACEi or ARB is synergistic and usually very effective at lowering BP; it is restricted to non-high performance aircraft. Calcium channel antagonists (specifically coat-core and GITS [Adalat CC® and Procardia XL®, respectively] and amlodipine [Norvasc®]) are also approved in aviators; whether used alone or in combination they are restricted to non-high performance aviators. Beta-blockers (specifically atenolol) may be used in the setting of a specific indication. (Beta-blockers are often poorly tolerated in aviators due to fatigue, reduced exercise capacity, and impotence; whether used alone or in combination they are restricted to non-high performance aviators.) Medical therapy for

hypertension other than that noted at the beginning of this paragraph <u>does require</u> a waiver for continued flying or special duty activities.

| ICD9 codes for hypertension |                                    |
|-----------------------------|------------------------------------|
| 401.0                       | Malignant essential hypertension   |
| 401.1                       | Benign essential hypertension      |
| 401.9                       | Unspecified essential hypertension |
| 405.0                       | Malignant secondary hypertension   |
| 405.1                       | Benign secondary hypertension      |
| 405.9                       | Unspecified secondary hypertension |

| ICD-10 codes for hypertension             |                                  |
|---|----------------------------------|
| I10                                       | Essential (primary) hypertension |
| I15.8                                     | Other secondary hypertension     |
| I15.9 Secondary hypertension, unspecified |                                  |

#### V. References.

- 1. Chobanian AV, Bakris GL, Black HR, et.al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC VII Express. National Heart, Lung, and Blood Institute. NIH, August 2004: 04-52303.
- 2. Hajjar I and Kotchen TA. Trends in Prevalence, Awareness, Treatment, and Control of Hypertension in the United States, 1988-2000. JAMA, 2003; 290: 199-206.
- 3. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet, 2002; 360: 1903-13.
- 4. Strader JR, Gray GW, and Leding CJ. Clinical aerospace cardiovascular medicine. Ch. 13 in Davis JR, Johnson R, Stepanek J, and Fogarty JA, eds. *Fundamentals of Aerospace Medicine*, 4th ed. Lippincott Williams & Wilkins, 2008.
- 5. Sytkowski PA, D'Agostino RB, Belanger AJ, et al. Secular Trends in Long-term Sustained Hypertension, Long-term Treatment and Cardiovascular Mortality. The Framingham Heart Study 1950 to 1990. Circulation, 1996; 93: 697-703.
- 6. Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomized trials. Lancet, 2003; 362: 1527-35.
- 7. Victor RG. Arterial hypertension. Ch. 67. in *Goldman's Cecil Medicine*, 24<sup>th</sup> ed., Saunders, 2011.
- 8. James PA, Oparil S, Carter BL, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Members Appointed to the Eighth Joint National Committee (JNC8). JAMA, 2013; published online 18 Dec 2013.

# Hyperthyroidism (Dec 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

Significant Changes: Waiver guide restructured. Waiver potential updated. Table 1 updated.

#### I. Waiver Consideration

All flying classes, ATC, and special warfare personnel diagnosed with subclinical hyperthyroidism or overt hyperthyroidism independent of the etiology, need for chronic maintenance therapy, and/or treatment with definitive therapy such as radioactive iodine ablation or thyroidectomy require aeromedical waiver. Hyperthyroidism that does not respond to treatment or that requires ongoing specialty care more often than annually is also disqualifying for all classes (including GBO) and for retention. The underlying disease process driving the hyperthyroid state requires appropriate medical attention, and should be clearly identified in the waiver package. Hyperthyroidism may be waivered on case-by-case basis following ACS review.

An initial aeromedical waiver can be considered once the underlying etiology has been addressed, and the individual demonstrates a clinical and biochemical euthyroid state. All personnel, including GBO, requiring current use of thionamide drugs (propylthiouracil or methimazole) are considered disqualified and will not generally be entertained for waiver. If definitive treatment with radioactive iodine ablation or thyroidectomy is completed, individuals warrant monitoring for the development of hypothyroidism. The need for thyroid replacement medication is potentially disqualifying. Please refer to the *Hypothyroidism* waiver guide.

Table 1: Waiver potential for subclinical or overt Hyperthyroidism

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------|------------------|--------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | Yes                      |
| FC II/III         | Yes <sup>1</sup> | MAJCOM           | Yes                      |
| GBO/ATC/SWA       | Yes <sup>1</sup> | MAJCOM           | Yes                      |

<sup>1.</sup> Wavier consideration is based on the underlying etiology of the hyperthyroidism and demonstration of a clinical and biochemical euthyroid state. The current use of thionamide drugs to maintain a euthyroid state will not generally be entertained for waiver.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. Describe episodes, including symptoms, duration, and frequency of events
    - i. Pertinent negative symptoms (eye, heart, psychiatric) must be reported as well as any current symptoms.
  - b. List all treatments and their effectiveness
  - c. Document the specific etiology (i.e., Grave's disease, TMNG, etc.)
- 2. Consultation reports from all treating providers or specialists, which should include:
  - a. Subjective symptoms and objective physical exam findings
  - b. Documentation of the presence or absence of orbitopathy.
- 3. Results of all pertinent laboratory studies, including diagnostic and follow-up results. This most include at least two recent consecutive sets of serum TSH, total T3, and free T4 values in the normal range (drawn 4-6 weeks apart), and thyroid antibody results (if obtained). A post-treatment CBC and CMP must also be provided if thionamide drugs (propylthiouracil or methimazole) treatment occurred.
- 4. Radiology reports from all diagnostic or follow-up imaging studies. (e.g., thyroid ultrasound, RAIU scan, etc.)
- 5. Ophthalmology consultant note if any symptoms or signs of optic neuropathy or orbitopathy were present.
- 6. Current physical examination findings.
- 7. Any other pertinent information.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Documentation of clinical and biochemical euthyroid state including updated TSH, free T4, and total T3.
  - b. Plan for monitoring of recurrence.
- 2 Updated consultation reports from treating specialist.
- 3 Current physical examination findings.
- 4 Any other pertinent information.
- If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## **III. Aeromedical Concerns**

Subclinical and overt hyperthyroidism can be associated with a variety of clinical manifestations that are of aeromedical concern. The focus of these aeromedical concerns center upon the effects on the cardiopulmonary system, potential changes in neurological and behavioral status, and on treatment side effects. Cardiac manifestations (tachycardia, dysrhythmias) may cause sudden incapacitation. Neurocognitive effects such as impaired attention and memory, and psychiatric symptoms, such as subtle irritability, restlessness, emotional lability and anxiety, may result in subtle incapacitation. Patients with thyroid

orbitopathy may have difficulty with eye movements. Additionally, corneal damage or optic neuropathy can occur. Other symptoms of untreated hyperthyroidism of operational importance include heat intolerance, fatigue, weakness, and tremor. All of these could be safety hazards as well as detract from duty performance. Post-treatment, the major aeromedical concerns are recurrence of hyperthyroidism (mainly after discontinuation of thionamide therapy) and the insidious onset of hypothyroidism, which can lead to apathy, slowed mentation, hypersomnolence, and performance degradation.

The use of thionamides for the treatment of hyperthyroidism is challenging operationally, since they are typically utilized for 6-18 months before discontinuation. Recurrence of hyperthyroidism after discontinuation of thionamides is high. Although long-term treatment with thionamides in select individuals to maintain a euthyroid state is a treatment strategy in some national guidelines, thionamides are not a definitive therapy for hyperthyroidism and require persistent monitoring (every 3-6 months) of thyroid levels with frequent dose adjustment to ensure a biochemical euthyroid state, which may not be possible in an operational setting. Since thionamides are not a definitive treatment, there is an aeromedical concern of breakthrough thyrotoxicosis while on treatment. Thus, the preferred aeromedical management is to pursue definitive treatment with either radioiodine ablation therapy or thyroidectomy. Additionally, thionamides may cause side effects incompatible with aviation duties to include vertigo, drowsiness, liver dysfunction as well as agranulocytosis. There is no specific laboratory monitoring for development of agranulocytosis or hepatotoxicy while on therapy except for baseline CBC and liver function panel. Thionamides are not on the approved aircrew medication list, and waiver for hyperthyroidism temporarily controlled with these medications is unlikely. There are no specific aeromedical concerns with radioiodine ablation treatment or thyroidectomy as long as long-term thyroid hormone supplementation is maintained, and there were no acute complications from the respective treatment.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 16 individuals with an AMS containing the diagnosis of Hyperthyroidism. One individual (6%) was disqualified. A breakdown of the cases was follows: 0 FC I/IA cases, 3 FC II cases (0 disqualified), 11 FC III cases (1 disqualified), 2 ATC/GBC cases (0 disqualified), 0 MOD cases, and 0 RPA Pilot cases.

| ICD-9 codes for hyperthyroidism  |                                       |  |
|----------------------------------|---------------------------------------|--|
| 242.9                            | Thyrotoxicosis with or without goiter |  |
| ICD-10 codes for hyperthyroidism |                                       |  |
| E05.00                           | Thyrotoxicosis (hyperthyroidism)      |  |

## IV. Suggested Readings

1. De Leo S, Lee SY and Braverman LE. Hyperthyroidism. Lancet, 2016; 288(10047): 906-918.

- 2. Kahaly GJ, Bartalena L, Hegedus L, et al. 2018 European Thyroid Association Guideline for the management of Graves' Hyperthyroidisms. European Thyroid Journal. 2018; 7:167-186. https://www.karger.com/article/fulltext/490384
- 3. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid, 2016; 26(10): 1343-1421. <a href="https://www.ncbi.nlm.nih.gov/pubmed/27521067">https://www.ncbi.nlm.nih.gov/pubmed/27521067</a>

## Hypogonadism (Dec 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

Significant Changes: Content updated to reflect national guidelines.

#### I. Waiver Consideration

Hypogonadism is not specifically identified as a disqualifying diagnosis for aviation or special operator duties. However, the need for chronic (greater than 6 months) exogenous hormone therapy is disqualifying for all flying classes, GBO, ATC, and special warfare duties as well as for retention. Waiver requirements for hypogonadism treated with testosterone replacement generally follow the recommendations established in national guidelines. Factors that are considered when assessing suitability for waiver include whether an appropriate and thorough evaluation was completed and whether the treatment and monitoring are appropriate in the context of established national guidelines. The use of any medication not included on a career-field approved medication list is independently disqualifying and will be considered on a case-by-case basis.

An initial aeromedical waiver may be considered once an individual demonstrates tolerability of the testosterone replacement, has resolution of all initial presenting symptoms, and has completed appropriate laboratory monitoring. A diagnosis of hypogonadism is established by obtaining two separate morning testosterone levels that are less than 300 ng/dL in symptomatic individuals. Inappropriately normal or low levels of FSH/LH warrant further evaluation for secondary causes of hypogonadism. Secondary causes of hypogonadism should be excluded as many of these diseases are independently disqualifying and carry additional aeromedical risk. Individuals who do not meet diagnostic criteria for hypogonadism on testosterone replacement are unlikely to receive a waiver.

Table 1: Waiver potential for Hypogonadism

| Flying Class (FC)          | Waiver Potential   | Waiver Authority    | ACS Review or Evaluation |
|----------------------------|--------------------|---------------------|--------------------------|
| FC I/IA                    | Yes <sup>1,2</sup> | AETC                | Yes                      |
| II/III                     | Yes <sup>1,2</sup> | MAJCOM <sup>3</sup> | No <sup>4</sup>          |
| GBO/ATC/Special<br>Warfare | Yes <sup>1,2</sup> | MAJCOM <sup>3</sup> | No <sup>4</sup>          |

- 1 Control of manifested symptoms is required before waiver submission.
- If the member has inappropriately normal or low FSH/LH in the setting of low testosterone, secondary causes of hypogonadism must be excluded as many of these diseases are independently disqualifying.
- 3 Use of any medication that is not included on the approved medication list is disqualifying, and the MAJCOM may disqualify the service member without AFMRA or ACS review. The waiver authority for all non-approved medications is AFMRA.
- 4 ACS review may be requested at the discretion of the waiver authority if there are clinical concerns.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

#### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- 2. Consultation reports form all treating providers or specialists, which should include:
  - a. Documentation of presenting symptoms and signs consistent with hypogonadism.
  - b. Current treatment plan, to include formulation and current dose of testosterone replacement, tolerance to prescribed therapies, and all appropriate laboratory monitoring (total testosterone, CBC, and PSA if > 40 years old)
- 3. All pertinent laboratory studies, including diagnostic and follow-up results.
  - a. Two or more pre-treatment, morning testosterone levels which should be less than 300 ng/dl.
  - b. Free testosterone, SHBG, and estrogen levels if indicated or obtained by treating provider.
  - c. FSH/LH levels and if low or inappropriately normal a secondary evaluation should be performed to include prolactin, TSH, ferritin, and iron saturation.
- 4. Radiology reports from all diagnostic or follow-up imaging studies.

- a. MRI of the pituitary is indicated in men with total testosterone levels of <150 ng/dL or when neurologic symptoms are present.
- 5. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 6. Current physical examination findings.
- 7. FL4 with RTD and ALC status.
- 8. Any other pertinent information.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Current symptoms and signs associated with hypogonadism.
  - b. Current medications, formulation, doses, and development of any adverse effects.
  - c. Current physical examination findings.
- 2 Consultation reports from treating specialist if applicable including current monitoring and treatment plan.
- 3 All interval monitoring labs including updated CBC and testosterone levels.
- 4 Any other pertinent information.
- 5 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Hypogonadism is a relatively common condition defined by a deficiency of testosterone hormone and/or a deficiency of the normal number of spermatozoa due to pathology at one or more levels of the hypothalamic-pituitary-testicular axis. Suggestive symptoms and signs of hypogonadism include reduced libido, decreased spontaneous erections, erectile dysfunction, infertility, loss of axillary and pubic hair, and hot flashes. Nonspecific symptoms and signs associated with hypogonadism include decreased energy, decreased motivation, depressed mood, sleep disturbances, decreased muscle mass and strength, and weigh gain. Studies have shown that up to one third of men diagnosed with hypogonadism do not meet diagnostic criteria for hypogonadism. Thus, it is important that individuals suspected of having hypogonadism be adequately evaluated prior to initiation of testosterone replacement. The diagnosis of hypogonadism is made in symptomatic individuals with two total testosterone measurements less than 300 ng/dL that were obtained on separate occasions in the early morning. Once a diagnosis of hypogonadism is established, LH and FSH should be obtained to determine whether the cause of hypogonadism is primary versus secondary. If the LH/FSH is low or inappropriately normal, further evaluation for secondary causes should be initiated since many of these diseases are independently disqualifying and carry additional aeromedical risk.

The adverse effects of exogenous testosterone therapy replacement include increased risk of potentiating an undiagnosed prostate cancer, worsening lower urinary tract symptoms, exacerbating untreated sleep apnea, and developing secondary polycythemia. The use of exogenous testosterone therapy has not been demonstrated to increase the risk of

developing a cardiovascular event in individuals with hypogonadism. In fact, low testosterone levels are associated with increased incidence of major adverse cardiac events. Thus, individuals diagnosed with hypogonadism should be adequately screened for cardiovascular risk factors. Multiple testosterone formulations are available. The use of implantable testosterone pellets are not approved for use in USAF personnel, but transdermal and injectable preparations are often considered for waiver. Transdermal patches, gels, and foams might cause skin irritation at the site of application. Intramuscular injectable formulations potentially increase risk of supraphysiologic testosterone levels. Additionally, injectable formulations pose mobility and readiness challenges in the deployed setting.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 158 individuals with an AMS containing the diagnosis of Hypogonadism. Seventeen individuals (10.8%) were disqualified. A breakdown of the cases was follows: 3 FC I/IA cases (2 disqualified), 71 FC II cases (3 disqualified), 57 FC III cases (9 disqualified), 19 ATC/GBC cases (2 disqualified), 5 MOD cases (0 disqualified), and 3 RPA Pilot cases (1 disqualified).

| ICD-9 codes for Hypogonadism |                               |  |
|------------------------------|-------------------------------|--|
| 257.2                        | Other testicular hypofunction |  |

| ICD-10 codes f | or Hypogonadism         |
|----------------|-------------------------|
| E29.1          | Testicular hypofunction |

# **IV. Suggested Readings**

- 1. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism*. 2018; 103(5):1715-1744. https://academic.oup.com/jcem/article/103/5/1715/4939465
- 2. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. The Journal of Urology. 2018; 200(2):423-432. https://www.auajournals.org/doi/10.1016/j.juro.2018.03.115
- 3. Park HJ, Ahn ST, and Moon DG. Evolution of Guidelines for Testosterone Replacement Therapy. Journal of Clinical Medicine. 2019; 8(3):410. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6462962/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6462962/</a>

## Hypothyroidism (Feb 2019)

Authors/Reviewers: Dr. Christopher Keirns, Maj Laura Bridge, and Capt Luke Menner (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Aerospace Medicine); and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: None.

#### I. Waiver Consideration

All flying classes and ATC/ SWA personnel utilizing thyroid replacement medication for the diagnosis of hypothyroidism require aeromedical waiver. Provided that the underlying causative etiology is not otherwise disqualifying, GBO personnel utilizing thyroid replacement medication only require grounding while symptomatic. Hypothyroidism that does not respond to treatment or that requires ongoing specialty care more often than annually is disqualifying for retention as well as for all flying classes, ATC, GBO, and SWA personnel. For all causes of hypothyroidism other than primary autoimmune hypothyroidism, the underlying disease process requires appropriate medical attention and a waiver request should be submitted in accordance with the applicable section of the waiver guide.

An initial aeromedical waiver can be considered once an individual demonstrates tolerability of the thyroid replacement medication and resolution of all initial presenting symptoms. In asymptomatic individuals, waiver requests may be considered prior to complete biochemical recovery (i.e., normalization of thyroid stimulating hormone [TSH]). Aeromedical waiver renewal will require re-confirmation that the service member remains clinically euthyroid (i.e., asymptomatic). Demonstration of a biochemical euthyroid state is desirable at the time of waiver renewal requests (i.e., recent normal TSH, +/- free thyroxine [free T4]). Titration or interval dosage changes of thyroid replacement medication(s) for the purpose of maintaining a biochemical euthyroid state does not require a new aeromedical waiver in the absence of any other clinical changes. DNIF/DNIC/DNIA may be necessary in the event that a person on exogenous thyroid replacement develops new symptoms of over- or under-treatment. Return to status can be granted when a clinical euthyroid state is re-established. Initiation of a new thyroid replacement medication that is not on the approved medication list requires DNIF/DNIC/DNIA and reconsideration regarding the need for a new aeromedical waiver.

Table 1: Waiver potential for hypothyroidism controlled on thyroid replacement therapy

| Flying Class<br>(FC) | Waiver<br>Potential <sup>1</sup> | Waiver<br>Authority | ACS Review or<br>Evaluation |
|----------------------|----------------------------------|---------------------|-----------------------------|
| FC I/IA              | Yes                              | AETC                | No                          |
| FC II/III            | Yes <sup>2</sup>                 | MAJCOM              | No                          |
| ATC/SWA              | 103                              | IVIAJCOIVI          | 110                         |
| GBO                  | $N/A^3$                          | N/A                 | N/A                         |

- 1. Untrained assets may be eligible for waiver.
- 2. Certification authority for untrained applicants is AETC.
- 3. DNIF/DNIA until all symptoms resolved. Primary autoimmune hypothyroidism and levothyroxine use are not disqualifying for GBO personnel. Other causative etiologies of hypothyroidism may be disqualifying.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

# A. <u>Initial Waiver Request:</u>

- 1. Information to include in history:
  - a. Subjective symptoms and objective physical exam findings to include examination of thyroid gland and lymph nodes of the head and neck
  - b. Complete list of all therapies, including all current medications with dates of initiation, doses, and all adverse effects
  - c. Documentation of underlying causative etiology of hypothyroidism
- 2. Consultation reports from all treating providers or specialists, which should include:
  - a. Description of whether individual is clinically euthyroid (i.e., are there any residual symptoms of hypothyroidism)
  - b. Assessment for medication side effects
  - c. Discussion of medication tolerance and adherence
  - d. Plan for monitoring serum TSH concentrations after initiation of thyroid replacement medication and after each dose adjustment
- 3. Laboratory studies required:
  - a. Serum TSH and free T4 prior to treatment
  - b. Serum TSH and free T4 after treatment initiation (if available)
  - c. All other laboratory and imaging studies ordered by treating provider(s) or consulting specialist(s), if performed. These results may include serum thyroid peroxidase (TPO) antibodies, ultrasonography, radioactive iodine scan, and/or fine-needle aspiration.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Subjective symptoms and objective physical exam findings to include examination of thyroid gland and lymph nodes of the head and neck
  - b. Complete list of current medications with dates of initiation, dates of dose changes, and all adverse effects
- 2 All interval consultation reports from all treating providers or specialists, which should include:
  - a. Description of whether individual is clinically euthyroid (i.e., are there any residual symptoms of hypothyroidism)
  - b. Assessment for medication side effects
  - c. Discussion of medication tolerance and adherence
  - d. Plan for continued monitoring of serum TSH concentrations
- 3 Laboratory studies required:
  - a. Updated serum TSH and free T4
  - b. All other laboratory and imaging studies ordered by treating providers or consulting specialist(s), if performed
- If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### **III. Aeromedical Concerns**

Hypothyroidism and subclinical hypothyroidism are relatively common conditions defined by a deficiency of thyroid hormone. The clinical presentation of hypothyroidism is highly variable and depends upon the severity of thyroid hormone deficiency and the speed at which the deficiency develops. Common symptoms include fatigue, cold intolerance, weight gain, constipation, dry skin, myalgia, loss of libido in both men and women, menstrual irregularities in women, and erectile dysfunction in men. Mental slowness, depression, apathy, headache, arthralgias, myalgias, dyspnea on exertion, hair thinning/hair loss, and hoarseness can also occur. Symptoms of hypothyroidism are less prominent clinically and better tolerated when there is a gradual loss of thyroid function (as in most cases of primary autoimmune hypothyroidism) compared to the rapid onset of hypothyroidism that occurs following surgical thyroidectomy or radioactive iodine ablation.

An appropriate laboratory evaluation includes measurement of TSH and free T4 levels. An elevated TSH indicates the presence of primary hypothyroidism, while a low free T4 confirms a biochemical hypothyroid state. In the case of subclinical hypothyroidism, TSH is elevated above the reference range, but the free T4 is normal. Secondary (central) hypothyroidism is diagnosed when the serum free T4 concentration is abnormally low and the serum TSH concentration is not appropriately elevated. Central hypothyroidism results from inadequate TSH secretion, which can be caused by either acquired or congenital disorders of the hypothalamus or pituitary gland.

The major aeromedical concern associated with hypothyroidism is the insidious nature of the disease, which may delay a diagnosis until symptoms become significant enough to

pose a potential threat to flying/operational safety. For this reason, close monitoring of patients with hypothyroidism or subclinical hypothyroidism is essential. Importantly, improvement in the clinical symptoms of hypothyroidism can occur relatively quickly after the initiation of thyroid replacement therapy, although complete biochemical recovery may take up to several months.. Generally, TSH does not reach steady-state for at least 6 weeks following initiation or dose adjustment of exogenous thyroid hormone. However, an aeromedical waiver request can be initiated once a clinically euthyroid state is documented by the treating physician (i.e., the individual is asymptomatic). Asymptomatic subclinical hypothyroidism is not disqualifying, but repeat thyroid function tests (TSH and free T4) should be obtained at least annually.

Review of AIMWTS data in Oct 2018 revealed a total of 1,316 waiver packages containing the diagnosis of hypothyroidism. Of that total, 39 were FC I/IA (10 disqualified), 533 were FC II (36 disqualified), 16 were RPA (3 disqualified), 582 were FC III (64 disqualified), 107 were ATC/GBC (13 disqualified), and 39 were MOD (1 disqualified). Of the 127 disqualifications, only 19 were specific to the diagnosis of thyroid disease. Fifteen were disqualified for either non-adherence to medications or poor control of their hypothyroidism. Three were disqualified for metastatic thyroid carcinoma or due to surgical complications that were determined to be incompatible with continued flying or special duties.

| Common ICD-9 codes used for Hypothyroidism |                                |  |
|--|--------------------------------|--|
| 243  | Congenital hypothyroidism      |  |
| 244  | Acquired hypothyroidism        |  |
| 246  | Other disorders of the thyroid |  |

| Common ICD-10 codes used for Hypothyroidism |  |  |
|---|--|--|
| E03.1                                       | Congenital hypothyroidism without goiter |  |
| E03.9                                       | Hypothyroidism, unspecified              |  |
| E07.89                                      | Other specified disorders of the thyroid |  |

## **IV. Suggested Readings**

- 1. American Thyroid Association (ATA) Professional Guidelines: <a href="https://www.thyroid.org/professionals/ata-professional-guidelines/">https://www.thyroid.org/professionals/ata-professional-guidelines/</a>
- 2. American Thyroid Association (ATA): 2014 Guidelines for the treatment of hypothyroidism. <a href="https://www.liebertpub.com/doi/pdf/10.1089/thy.2014.0028">https://www.liebertpub.com/doi/pdf/10.1089/thy.2014.0028</a>
- 3. The American Association of Clinical Endocrinologists Clinical Practice Guidelines: <a href="https://www.aace.com/publications/guidelines">https://www.aace.com/publications/guidelines</a>
- 4. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid 2012; 22:1200. https://www.aace.com/files/final-file-hypo-guidelines.pdf

- 5. Rugge JB, Bougatsos C, Chou R. Screening and treatment of thyroid dysfunction: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2015; 162:35.
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## **Implantable Collamer Lens (ICL) Surgery (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Lt Col Richard Townley (SG Consultant for Refractive Surgery), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** ICL surgery is now authorized for trained USAF aircrew. Refractive error limits must be within waiver tolerances of other laser refractive surgical procedures. MSD C33, 34, and 59.

#### I. Waiver Consideration

Implantable collamer lens implantation surgery is disqualifying for Flying Class I, IA, II, III, GBO (RPA Pilot only), and SWA duties. There is waiver potential for FC II (non-pilot), FC III, GBO (RPA Pilot), and Special Warfare Airfare Airmen (SWA). ICL implantation surgery is not yet approved for FC II (pilots). It is not disqualifying for ATC, GBO (RPA SO and MOD), and Operational Support Flying Duty (OSF) personnel. No waivers will be considered for FC I/IA at this time, regardless of outcome. Implantation of phakic intraocular lenses other than the ICL is not authorized.

For ATC, GBO (RPA SO and MOD), and OSF personnel, a history of ICL surgery is only disqualifying if the surgical outcome results in the member's inability to meet visual standards for the career field.

Active duty members may have surgery at any DoD Refractive Surgery center. Members not eligible for TRICARE medical benefits (ANG/AFRC) may go to a civilian provider. Please submit for waiver once the member is one month post-op from surgery, meets vision standards, and all complications (if any) are appropriately managed and resolved.

**Table 1: Waiver potential for ICL surgery** 

| Flying Class (FC)                | Waiver<br>Potential | Waiver<br>Authority | ACS Review/Evaluation |
|----------------------------------|---------------------|---------------------|-----------------------|
| FC I/IA                          | No                  | AETC                | No                    |
| FC II (pilot)                    | No                  | MAJCOM              | No                    |
| FC II (non-pilot)/<br>SWA/FC III | Yes                 | MAJCOM              | Yes                   |
| ATC/GBO/OSF                      | N/A <sup>1</sup>    | MAJCOM              | No                    |

<sup>1.</sup> ICL surgery is only disqualifying for ATC/GBO/OSF if the surgical outcome results in the member's inability to meet established vision standards or interferes with the member's ability to perform his/her duties.

Table 2: Pre-ICL Cycloplegic Refractive Error Limits<sup>1,2</sup>

| Myopia (Most myopic meridian)       | ≤ -10.00 Diopters |  |
|-------------------------------------|-------------------|--|
| Hyperopia (Most hyperopic meridian) | ≤ +4.00 Diopters  |  |
| Astigmatism                         | ≤ 3.00 Diopters   |  |

<sup>1.</sup> ICL surgery is NOT authorized outside of these refractive error limits, however members who have a pre-existing waiver for refractive error beyond these limits will be considered for ICL surgery on a case-by-case basis.

**Table 3: Waiverable Examination Results** 

| Examination                            | Waiverable Results                                   |
|--|--|
| Best corrected visual acuity (OVT)     | 20/20 or better each eye                             |
| Precision Vision 5% low contrast chart | 20/50 or better each eye                             |
| Refractive error                       | Stable, no more than 0.50 diopter shift in           |
|  | manifest sphere or cylinder refractive power         |
|  | between two readings at least 2 weeks apart          |
| Intraocular Pressure                   | ≤21 mmHg   |
|  |  |
| Depth perception (OVT-DP)              | Line B or better. If fails, refer to defective depth |
|  | perception/stereopsis waiver guide.                  |
| ICL Vault                              | Greater than or equal to 20% corneal thickness       |
|  | based on slit lamp measurements or 100 microns       |
|  | based on anterior segment OCT measurements.          |
| Slit Lamp Exam                         | Open angles and no cataract formation.               |
| Fundus Exam                            | No new or previously unrecognized retinal            |
|  | pathology.   |

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

To be eligible for ICL surgery, the member must first be disqualified for PRK/LASEK/LASIK surgery and be granted a permission to proceed letter from the Aviation Program Manager (APM) located at Wright-Patterson AFB. The member must then be examined by an ophthalmologist who has been certified in ICL surgery to make the final determination of surgical candidacy. After the surgery, the surgeon will evaluate the member for their one day, one week, and one month examinations. The three month, six month, and twelve month follow-up appointments, may be accomplished by a refractive surgeon or certified optometric co-manager to meet RS standard of care requirements. Any abnormalities or concerns found should be immediately reported to the surgeon to expedite evaluation and intervention. After the 12 month postoperative appointment, annual routine Flight or Special Operational Duty Qualification (PHA) and vision (optometry or ophthalmology) exams will be required. Waiver submission may be

<sup>2.</sup> ICL implant choice must be a currently FDA approved implant (ICLs for hyperopia are not yet FDA approved).

accomplished once the member is one month post-op from surgery, meets vision standards, and all complications (if any) are appropriately managed and resolved.

The aircrew member will be placed on non-mobility status, restricting the individual from deployment via AF Form 469 for a minimum of one month after surgery, even if no longer on steroid eye drops.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. Pre-op cycloplegic refraction.
  - b. Surgical procedure, date, location.
  - c. Assessment (negative and positive) of post-op symptoms of glare, halos, reduced night vision and diplopia.
  - d. Eye medications usage, past and current, include discontinuation date
- 2. Physical (Current):
  - a. Uncorrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
  - b. Best corrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
  - c. Cycloplegic refraction and dilated fundus exam.
  - d. Two post-op refractions at least 2 weeks apart that shows stability (no more than
  - 0.50 diopter shift in **manifest** sphere or cylinder power).
  - e. Slit lamp exam.
  - f. Intraocular pressures (IOPs).
  - g. Depth perception (OVT-DP). (If fails and previously waived for defective depth perception using AO Vectograph, then include AO Vectograph).
  - h. ICL vault determine by slit lamp measurement and/or anterior segment OCT.
  - i. Endothelial cell count (pre-operative and post-operative measurements), if available.
- 3. Attach copy of "Permission to Proceed" letter.
- 4. Attach copy of the operative report for each eye treated, post-RS evaluations (1, 3, 6, 12 months post-op and annually, and any other additional follow-ups) and any RS-related incidents.
- 5. If any of the above requested items cannot be provided, please provide an explanation to the waiver authority in the AMS why that could not be provided.

#### B. Waiver Renewal Request:

- 1 History:
  - a. Pre-op cycloplegic refraction.
  - b. Surgical procedure, date and location.
  - c. Assessment (negative and positive) of post-op symptoms of glare, halos, reduced night vision and diplopia.
  - d. Eye medications usage, past and current.

## 2 Physical (current):

- a. Uncorrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
- b. Best corrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
- c. Manifest refraction
- d. Slit lamp exam noting stability of the lens, patency of the peripheral iridotomy, and

presence or absence of postoperative cataract formation.

- e. Intraocular pressures (IOPs)
- f. Depth perception (OVT-DP). (If fails and previously waived for defective depth perception using AO Vectograph, then include AO Vectograph).
- g. ICL vault determine by slit lamp measurement and/or anterior segment OCT.
- h. Endothelial cell count (pre-operative and post-operative measurements), if available.
- 3 If any of the above requested items cannot be provided, please provide an explanation to the waiver authority in the AMS why that could not be provided.

#### III. Aeromedical Concerns

Implantable collamer lens implantation is a refractive surgery involving implantation of an artificial lens on top of the natural lens for individuals who are not candidates for traditional laser refractive surgical procedures (PRK, LASEK, or LASIK). While the FDA has approved much higher levels of myopia, current Air Force policy allows treatment with ICL surgery in aircrew with refraction from -3.00 D to -10.00 D. With ICL surgery, the major concerns are quality of visual outcome, postoperative cataract formation, pupillary block glaucoma, and endothelial cell loss causing corneal edema.

An independent Air Force Surgeon General directed review was conducted at Wilford Hall to determine the safety and efficacy of the ICL in Air Force personnel from 2016-2018. Even though the implantable collamer lenses used at the time did nothing to correct for astigmatism, 100% achieved uncorrected vision 20/30 or better without glasses. In terms of cataract formation, a meta-analysis reviewed 15 studies involving a total of 1,387 eyes and found an overall incidence of 0.3%.

The risk of pupillary block glaucoma is mitigated by proper ICL sizing to ensure a vault less than 1000 microns as well as the creation of a peripheral iridotomy for current FDA approved models. Newer models, such as the EVO (pending FDA approval), have a central port created in the lens, which negates the need for a peripheral iridotomy.

Endothelial cell loss is a known complication of intraocular surgery and happens to a greater extent the closer a lens implant is placed in relation to the endothelial cells. The initial FDA trials indicated an annual endothelial cell loss as high as 2.47% per year that was felt to continue indefinitely. More recent studies demonstrate cumulative losses are

lower than the earlier FDA trials and indicate no corneal adverse events were noted in any of the studies, which indicates that this risk is not as concerning as it initially appeared.

| ICD-10 Co  | ICD-10 Codes for Corneal Refractive Surgery             |  |  |
|------------|---|--|--|
| H52.0      | Hypermetropia, right, left, both                        |  |  |
| 1, 2, 3    |   |  |  |
| H52.1      | Myopia, right, left, both                               |  |  |
| 1, 2, 3    |   |  |  |
| H52.20     | Unspecified astigmatism, right, left, both, unspecified |  |  |
| 1, 2, 3, 9 |   |  |  |
| Z96.1      | Presence of intraocular lens                            |  |  |

# **IV. Suggested Readings**

- 1. Dougherty PH and Priver T. Refractive outcomes and safety of the implantable collamer lens in young low-to-moderate myopes. Clin Ophthalmol, 2017: 11: 273-77.
- 2. Packer M. Meta-analysis and review: effectiveness, safety, and central port design of the intraocular collamer lens. Clin Ophthalmol, 2016; 10: 1059-77.
- 3. Sander DR. Anterior Subcapsular Opacities and Cataracts 5 Years After Surgery in the Visian Implantable Collamer Lens FDA Trial. JRefract Surg, 2008: 24(6): 566-70.
- 4. Zeng Q, Xie X, Chen Q. Prevention and management of collagen copolymer phakic intraocular lens exchange; causes and surgical techniques. J Cataract Refract Surg, 2015; 41: 576-84.
- 5. Food and Drug Administration. Summary of safety and effectiveness data, STAAR Visian ICL. Date of Notice of Approval: December 22, 2005. Available from: http://www.accessdata.fda.gov/cdrh\_docs/pdf3/P030016b.pdf. Accessed July 2, 2019.
- 6. Moya T, Javaloy J, Montes-Mico R, et al. Implantable Collamer lens for myopia: assessment 12 years after implantation. J Refract Surg, 2015; 31(8): 548-56.
- 7. Igarashi A, Shimizu K, and Kamiya K. Eight-Year Follow-up of Posterior Chamber Phakic Intraocular Lens Implantation for Moderate to High Myopia. Am J Ophthalmol, 2014; 157(3): 532-39.
- 8. Alfonso JF, Baamonde B, Fernandez-Vega L, et al. Posterior chamber collagen copolymer phakic intraocular lenses to correct myopia: five-year follow-up. J Cataract Refract Surg, 2011: 37(5): 873-80.

#### WAIVER GUIDE

Updated: Mar 2016

Supersedes Waiver Guide of Jan 2013

By: Dr Dan Van Syoc

Reviewed by: Col Pat Storms, AF/SG consultant for gastroenterology

#### **CONDITION:**

Irritable Bowel Syndrome (May 2016)

#### I. Waiver Consideration.

IBS requiring treatment beyond dietary modifications is disqualifying for all classes of Air Force flying to include ATC/GBO and SWA personnel, as well as for retention. Due to the chronic and unpredictable nature of the disease, it is not wise to consider aviation applicants with the history of IBS for any flying class or position. These folks do not fare well with many stressful positions and run the risk of not being available, on short notice, for many sorties. For trained aviators with mild symptoms easily treatable with diet or other non-pharmacologic therapies, waiver can be considered. There are some cases that can be controlled on approved medications and diets; these aviators can also be considered for a waiver.

Table 1: Waiver potential for Irritable Bowel Syndrome NOT controlled by dietary modifications alone

| Flying Class (FC)   | Waiver Potential#<br>Waiver Authority | ACS Evaluation or<br>Review* |
|---|---------------------------------------|------------------------------|
| I/IA  | No<br>AETC                            | No                           |
| II/III - trained  | Yes<br>MAJCOM                         | Yes                          |
| II – untrained<br>(initial Flight<br>Surgeon and RPA<br>operator applicants)<br>and III - untrained | No<br>AETC                            | Maybe                        |
| ATC/GBO<br>SWA  | Yes<br>MAJCOM                         | No                           |

<sup>\*</sup>ACS review is at the discretion of the waiver authority in cases where the diagnosis is uncertain. # No indefinite waivers.

AIMWTS review in Oct 2015 resulted in 283 cases with the diagnosis code of IBS. There were a total of 136 disqualifications which is 48% of all submitted cases. Breakdown of the cases revealed: 11 FC I/IA cases (9 disqualified), 80 FC II cases (27 disqualified), 150 FC III cases (82 disqualified), 18 ATC/GBC cases (11 disqualified), and 24 MOD cases (7 disqualified). With IBS there are significant comorbidities that are associated with the disease. In many cases it is difficult to determine if the comorbidities contribute to the IBS or are the comorbidities a result of having IBS.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

AMS for <u>initial waiver</u> for irritable bowel syndrome must include the following:

- A. History specifically discussing the disease entity, frequency of events, specific symptoms, what relieves symptoms, pattern of recurrence, duration of attacks, and treatments (both pharmacologic and non-pharmacologic) used with their effectiveness.
- B. Results of all labs and imaging tests, if performed.
- C. Clinical consultation report from a gastroenterologist or internist.
- D. Documentation that the aviator is asymptomatic off all daily medications, or is stable on medications currently on the approved medication list.
- E. Results of MEB if applicable.

AMS for <u>waiver renewal</u> for irritable bowel syndrome must include the following:

- A. Interim history specifically discussing any recurrences or any changes in the disease pattern and all treatments used.
- B. Testing: new labs and imaging results, if ordered, since last waiver.
- C. Clinical consultation report from a gastroenterologist or internist unless aviator has been totally asymptomatic since last waiver.
- D. Documentation that the aviator's condition is stable and that he or she is not on unapproved medication.

#### III. Overview.

Irritable bowel syndrome (IBS) is a common malady that is characterized by the presence of abdominal discomfort or pain associated with disturbed defecation. It is important to note that IBS is not a single disease but rather a symptom cluster resulting from diverse pathologies.<sup>1</sup> IBS patients may experience constipation, diarrhea, or a combination of these symptoms. The prevalence of IBS depends on the case definition used and the setting (specialist vs. primary care) from which the subjects are chosen. When employing the Rome criteria, IBS is thought to have a prevalence of up to 12 % in the US population.<sup>2</sup> IBS patients often utilize health services more than those without IBS for gastrointestinal (GI) symptoms as well as for non-GI concerns. It has been estimated that 25-50% of all referrals to gastroenterologists and an estimated health care expenditure of \$30 billion dollars a year can be attributed to IBS (2012 data).<sup>3</sup>

The pathophysiology of IBS is a subject of ongoing debate, but abnormal colonic and small bowel motility and visceral hypersensitivity are commonly cited as having pathophysiologic significance.<sup>2</sup> Additional considerations include alterations in central autonomic regulation, subclinical mucosal inflammation, and even a potential role for intestinal microbiota. In fact, a significant proportion of subjects (7-31%) recovering from infectious gastroenteritis develop post-infectious IBS, dyspepsia, or both.<sup>4</sup> While the mechanisms of post-infectious IBS are unclear, persistent mucosal inflammation in these

IBS patients could be the result of inefficient down-regulation of the inflammatory response to infection. Intestinal dysmotility can also lead to altered clearance of small bowel microbial flora, and studies have attempted to link small bowel bacterial overgrowth to IBS. Though convincing evidence is still lacking, the potential connection has prompted treatment regimens that include neomycin and rifamixin, both non-absorbable antibiotics that target gut flora.<sup>2, 5</sup>

Patients with IBS can present with a wide array of symptoms which include both gastrointestinal and extra intestinal complaints. However, the symptom complex of chronic abdominal pain and altered bowel habits remains the nonspecific yet primary characteristics of IBS. The Rome III criteria, updated in 2005, are widely used as diagnostic criteria for IBS (Table 1). Coexisting psychological symptoms are common, primarily anxiety, somatization, and symptom-related fears, but it's not clear if these symptoms lead to IBS, or are a psychological response to the discomfort associated with IBS. The constellation of gut-focused symptomatology and co-morbid psychological issues can contribute to impairment in quality of life and overutilization of health care resources.<sup>6</sup> While not specifically cited as criteria within the Rome III classification scheme, the following are commonly reported by patients considered to have IBS: abnormal stool frequency (<3 bowel movements per week or >3 bowel movements per day); abnormal stool form (lumpy-hard stool or loose-watery stool); defecation straining; defecation urgency; a feeling of incomplete evacuation; passing mucus, and bloating. These symptoms, depending on their predominance, delineate subtypes of IBS, and are described as: IBS with diarrhea, IBS with constipation, mixed IBS and unsubtyped IBS. IBS also can be associated with non-GI complaints to include impaired sexual function, dysmenorrhea, dyspareunia, increased urinary frequency and urgency, and fibromyalgia.<sup>7</sup>

IBS is a diagnosis that can often be suggested by history alone. Empiric therapy is often initiated with a minimum of initial testing, reserving a more aggressive workup to those who present alarm features or fail to respond to conservative therapy. The most recent guidelines on the evaluation of IBS, published by the American College of Gastroenterology (ACG) IBS Task Force, encourage clinicians to make a positive diagnosis of IBS based on a thorough history, using symptom-based criteria. Testing should be held in reserve and used in conjunction with the presence or absence of specific alarm features such as rectal bleeding, unintended weight loss, iron deficiency anemia, family history of inflammatory bowel disease or colorectal cancer, family history of celiac disease, or nocturnal diarrhea.<sup>5</sup> Such testing might involve endoscopy to exclude visible mucosal pathology, testing for celiac disease, and breath tests to assess for the presence of small bowel bacterial overgrowth.<sup>5</sup>

The assessment and treatment of a patient with IBS can stress patients and physicians alike. The lack of a single definitive diagnostic test can lead to a patient undergoing a number of evaluations, only to be told that "all of your tests or normal, so this must all be in your head". The management of these patients is optimized by an individualized approach utilizing dietary, lifestyle, medical, and behavioral modalities. Likewise, the lack of effective pharmacologic therapy that is universally helpful and free of bothersome side effects is a source of additional stress. The most important component in the

treatment of IBS is the establishment of a therapeutic physician-patient relationship. The provider should be non-judgmental, establish realistic expectations with consistent limits, and involve the patient in all treatment decisions. Proper education of the patient is vital – patients need to be well informed of the chronic and benign nature of the disease, without trivializing their symptoms or the lifestyle impact of their IBS. The major goal of therapy is a reduction in the severity and frequency of symptoms and an overall improvement in their quality of life.<sup>8</sup> Treatment is divided into pharmacologic and non-pharmacologic methods with the latter favored by most practitioners as a starting point. Dietary therapy is frequently a first step, and while increasing dietary fiber has long been recommended as a treatment for IBS, there is little evidence to support the efficacy of fiber supplementation in IBS patients. In fact, Wilkins in a 2012 review of the management of IBS in adults cites a Cochrane review of 12 randomized controlled trials involving 621 IBS patients. The Cochrane review could find no evidence that fiber is effective for treating IBS.<sup>9, 10</sup> Fiber may have some utility in constipation-predominant IBS, but its benefits must be weighed against its potential to increase bloating and abdominal discomfort. Polyethylene glycol (PEG) laxative was shown to improve stool frequency but not abdominal pain. 11 In addition, foods that appear to routinely stimulate symptoms may need to be eliminated from the diet – some patients are greatly benefited by eliminating different sugars from their diet. Some physicians recommend the reduction or exclusion of food that increase flatulence – the explanation is that the underlying visceral hypersensitivity may explain the discomfort experienced by some patients after these foods.<sup>8</sup> Care should be taken to avoid an overly restrictive diet, since many IBS symptoms are random in their presentation and are unrelated to specific foods. Some patients, in their zeal to eliminate dietary triggers, may put themselves on nutritionally inadequate diets.

For some patients who associate their symptoms with stressors, behavioral treatment can be helpful. Therapies that are utilized include hypnosis, biofeedback, and psychotherapy. Advantages to these types of therapy are that they all involve the patient and give them an opportunity to take responsibility for their treatment plan. These types of therapy are most helpful in those patients who are very motivated and have symptoms that are more severe.<sup>12</sup>

For patients with moderate or severe symptoms, the provider needs to consider the use of medications. Antispasmodics such as hyoscyamine and dicyclomine are used frequently but efficacy for IBS has yet to be well established. Troubling side effects from these anticholinergic antispasmodics include visual disturbances, dry mouth, urinary retention and constipation, so they need to be used with caution (these side-effects prohibit their use in aviators). Laxatives are sometimes utilized in those patients with constipation-predominant IBS. These agents can include stool softeners such as docusate, colonic stimulants such as bisacodyl and senna and osmotic agents such as polyethylene glycol, magnesium-containing compounds, and lactulose. Care should be taken to avoid the routine use of cathartic laxatives, such as senna or bisacodyl, given the habit-forming nature of these laxatives. A newer medication, linaclotide has been given a good recommendation by the American Gastroenterology Association (AGA) for use in constipation-predominant IBS. <sup>14, 15</sup> For diarrhea-predominant IBS, loperamide has demonstrated good efficacy in reducing stool frequency, but is not generally helpful for

pain symptoms.<sup>13</sup> Particular care should be taken in patients with a mixed pattern of IBS, as their swings from constipation to diarrhea could be aggravated by therapeutic efforts to modify their bowel movement frequency.

Antidepressants have been shown to relieve pain at low doses. They work by modulating the perception of visceral pain. Tricyclic antidepressants have been studied most extensively, but large meta-analyses of their efficacy have shown variable results. <sup>11, 13</sup> A newer approach to the treatment of IBS involves the use of 5-HT modulators. These medications, which include tegaserod, a partial agonist of the 5-HT<sub>4</sub> receptor, and alosetron, a 5-HT<sub>3</sub> receptor antagonist, need to be used only by gastroenterologists who are very familiar with the proper indications for their use and with the problems associated with these medications. <sup>13</sup>

Several newer approaches have been assessed for efficacy in the treatment of IBS. Antibiotics and peppermint oil have shown promise in randomized control trials, while mast cell stabilizers have been slightly disappointing. One antibiotic of note, Rifaximin (Xifaxan®), is an oral rifamycin with no systemic bioavailability after oral ingestion. While used clinically for the treatment of travelers' diarrhea and hepatic encephalopathy, it has been studied in IBS patients without constipation. When used at a dose of 550 mg three times daily for two weeks, patients in the treatment group experienced significant relief of global IBS symptoms. <sup>16</sup> The AGA suggests using rifaximin over no drugs in patients with diarrhea-predominant disease. <sup>14, 15</sup> Complimentary approaches such as use of herbs, probiotics, acupuncture and enzyme supplementation all remain uncertain in their role for treating IBS. <sup>11</sup>

Table 2: Rome III diagnostic criteria\* for irritable bowel syndrome

Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months associated with 2 or more of the following:

- (1) Improvement with defecation
- (2) Onset associated with a change in frequency of stool
- (3) Onset associated with a change in form (appearance) of stool

#### IV. Aeromedical Concerns.

Urgency and frequency of defecation, as well as abdominal pain or discomfort, can be very distracting during flight. These can be further aggravated by the effects of rapid altitude changes in patients with abdominal distension, gas, and bloating. IBS symptoms can present inconveniences during long flights, extended trips, or austere living conditions and symptoms may likely worsen as a result of these types of stressors. There is also great concern with aviators afflicted with IBS due to its chronicity. If dietary therapy is deemed necessary, the nature of the flying mission may make it extremely inconvenient if not impossible to comply.<sup>17</sup> Many medications used for treatment of IBS symptoms cause cognitive impairment, anticholinergic effects, hypotension, or disorientation, and are thus not on the approved list of medications for flyers.

<sup>\*</sup> Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis. Discomfort means an uncomfortable sensation not described as pain.

| ICD-9 code for Irritable Bowel Syndrome |                          |
|---|--------------------------|
| 564.1                                   | Irritable Bowel Syndrome |

| ICD-10 code for Irritable Bowel Syndrome |   |  |
|--|---|--|
| K58.9                                    | Irritable Bowel Syndrome without diarrhea |  |

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# Keratoconus, Abnormal Corneal Topography, and Corneal Collagen Crosslinking (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: New Ground Based Operator (GBO) Standards. MSD C25, C30.

#### I. Waiver Consideration

Keratoconus (KCN), including similar ectatic corneal disorders to include Pelucid Marginal Degeneration (PMD) and Keratoglobus, is a disqualifying condition for all flying classes in the Air Force, to include GBO, ATC, and SWA, and is not waiverable FCI/IA, IFCII and IFCIII. (MSD C25 if progressive, C30 if stable). An FC I, IA, IFCII, and IFCIII waiver for abnormal corneal topography (MSD C30), which is a topography that is not normal but also not diagnostic of KCN is possible, will be considered on a case-by-case basis with ACS review. Abnormal corneal topography is not disqualifying for ATC, GBO, or OSF duties.

Contact lenses, if worn, must be fitted appropriately and achieve adequate wearing times prior to use while flying. Trained aircrew diagnosed with KCN require frequent evaluations and management to ensure that they are adequately corrected to mitigate the optical side effects of the condition. Although contact lenses, particularly rigid lenses, are frequently required to optimize vision performance in these cases, aircrew must also be adequately corrected with spectacle back-ups. A key element in correction of KCN is to ensure adequate stereopsis with both contact lenses and spectacles. Trained aircrew who require specialty contact lenses (e.g. rigid gas permeable, hybrid, scleral lens) to meet stereopsis standards may be granted a IIC waiver (restricted to flying with another qualified pilot) and must carry a back-up pair of both contact lenses and spectacles on person at all times while flying. Specialty contact lenses for KCN are fitted and dispensed by the ACS.

As discussed above, historically, treatment of KCN typically consists of correction of refractive error with spectacle or contacts (soft, rigid, or hybrid) until the patient no longer can be corrected with these modalities; that member may then require penetrating keratoplasty (corneal transplant surgery). A more recent treatment procedure was developed and FDA approved (2016) which utilizes Riboflavin (Vitamin B2) and ultraviolet light to polymerize stromal collagen and induce corneal stiffening, with the goal to halt progression of KCN. This method is known as collagen cross-linking (CXL) and has widespread use in Europe since 2003. Several studies have shown very promising results with reduction in corneal steepness, improved corrected visual acuity, and halting of progression of KCN.

There is a gain of one to three lines of best-corrected visual acuity ranging from 21-54% after CXL. In terms of safety, there is a loss of best-corrected visual acuity at a rate of 0-

2.9% and failure rates ranging from 0-7.6%. Larger studies have shown the overall failure rate to be at 1%.<sup>7</sup> Corneal haze can be seen after this procedure at a rate as high as 8.6%. However, Scheimpflug analysis following the natural history of post-CXL haze shows this to peak at one month postop with the majority of the return within the first three to six months and a near return to baseline by one year. This pattern of healing is very similar to that of PRK. Therefore, CXL shows incredible promise to help aircrew with keratoconus to see better while having an acceptable risk profile. The ACS will follow waived aircrew who have had CXL in a study group to determine if the aviation environment impacts the ultimate outcome and the best time postoperatively to return to flying status.

Table 1: Waiver potential for Keratoconus (MSD C25 if progressive, C30 if stable)

| Flying Class (FC)  | Waiver<br>Potential | Waiver<br>Authority <sup>2</sup> | ACS Review or Evaluation |
|--|---------------------|----------------------------------|--------------------------|
| FC I/IA, initial<br>FC II <sup>1</sup> , initial FC<br>III | No                  | AETC                             | N/A                      |
| FC II/FC III,<br>SWA                                       | Yes                 | MAJCOM                           | Yes                      |
| ATC, GBO, OSF  | Maybe <sup>3</sup>  | MAJCOM                           | Yes                      |

<sup>1.</sup> IFCII includes Flight Surgeons.

Table 2: Waiver potential for Abnormal Corneal Topography (MSD C30)

| Flying Class (FC)                            | Waiver Potential                         | Waiver Authority | <b>ACS Review or Evaluation</b> |
|--|--|------------------|---------------------------------|
| FC I   | Yes, if meets<br>REACT Study<br>Criteria | AETC             | Yes                             |
| FC IA, IFC III                               | Maybe <sup>1</sup>                       | AETC<br>AFMRA    | Yes                             |
| Initial FC II (FS),<br>FC II, FC III,<br>SWA | Yes <sup>1</sup>                         | MAJCOM           | Yes                             |
| ATC, GBO, OSF                                | N/A                                      | N/A              | N/A                             |

<sup>1.</sup> Any corneal findings that exceed the following criteria should be submitted for waiver: I-S > 1.4, corneal pachymetry < 475 microns by any device, steepest K > 48 diopters by any measurement, pachymetry progression > 1.2 on Belin-Ambrósio Enhanced Ectasia. Waivers will be considered on a case by case basis.

<sup>2.</sup> Cases that are progressive, require long-term treatment, surgical intervention or results in spectacle corrected visual acuity below that specified in the MSD require AFMRA waiver after RILO/MEB.

<sup>3.</sup> Condition only disqualifying if demonstrates progression, requires long term treatment or surgical intervention, or does not meet best spectacled correction standards; requires RILO/MEB prior to waiver submission.

**Table 3: Waiverable Postoperative CXL Examination Results** 

| Examination                            | Waiverable Results                           |  |
|--|--|--|
| Best corrected visual acuity (OVT)     | 20/20 or prior waivered baseline vision*     |  |
| Precision Vision 5% low contrast chart | 20/50 or prior waivered baseline vision*     |  |
| Slit lamp exam                         | No more than trace corneal haze*             |  |
| Refractive error                       | Stable, no more than 0.50 diopter shift in   |  |
|  | manifest sphere refractive power between     |  |
|  | two readings at least 2 weeks apart*         |  |
| Keratometry                            | Stable, no more than 0.50 diopter shift in   |  |
|  | steepest keratometry reading on CT or        |  |
|  | tangential view of pentacam.*                |  |
| Preoperative Corneal Pachymetry        | Corneal pachymetry > 400 microns             |  |
| Fundus exam                            | No new or previously unrecognized retinal    |  |
|  | pathology†                                   |  |
| Depth perception (OVT-DP)              | Line B. If fails, see substandard stereopsis |  |
|  | waiver guide.                                |  |

<sup>\*</sup> If outside these limits, refer to local eye care provider and/or treating surgery center prior to referral to ACS to ensure member is ready for ACS evaluation.

AIMWTS review in Jul 2018 revealed 434 aircrew with waiver dispositions for keratoconus or abnormal corneal topography. There were 94 FC I/IA cases, 157 FC II cases, 16 RPA pilot cases, 143 FC III cases, 16 ATC/GBC cases, and 8 MOD cases. There were a total of 141 disqualifications; 65 were FC I/IA, 9 FC II, 4 were RPA pilots, 56 FC III, 4 were ATC/GBC, and 3 were MOD.

#### II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. First-time waiver for KCN in trained aircrew or for abnormal corneal topography in aircrew or applicants requires an in-person ACS evaluation. Following first-time waiver, trained aircrew with KCN will be followed at the ACS every 1-3 years depending on clinical and optical stability. For those enrolled in the REACT study, an annual corneal evaluation including corneal topography and Orbscan or Pentacam, OVT-DP stereopsis, refraction to best visual acuity, and ultrasound central pachymetry (corneal thickness) is required with an ACS review prior to waiver renewal. If KCN or abnormal corneal topography demonstrates progression, requires long term treatment, surgical intervention or results in spectacle corrected visual acuity below the level specified in item MSD C2, MSD C25 applies(which also is a retention standard), and RILO/MEB results are required for inclusion into AMS submission.

#### A. Initial Waiver Request:

- 1. History of previous refractions and progression of astigmatism (if available) and other visual symptoms.
- 2. Family history of KCN and any impact on job/daily life.
- 3. Full eye exam to include:

<sup>†</sup> Work-up and submit waiver request for new diagnosis

- a. 5% Precision Vision chart.
- b. Manifest Refraction to best visual acuity.
- c. Corneal Topography. Submissions should be formatted in **Axial** view using a standard dioptric scale (39.0 to 50.0 Diopter range, 0.50 Diopter increments) and standard color palette. The **OD/OS Display** with an **Axial Map** and an **Axial Numeric View** is preferred. All ATLAS topographies should display the **Axial I-S** value.
- d. Retinoscopy findings (+/- scissoring).
- e. Slit Lamp Exam with comment on positive/negative findings in the cornea.
- 4. Orbscan or Pentacam (Holladay and Belin-Ambrósio), if available.
- 5. Ophthalmology consultation report in advanced cases.
- 6. Pre-operative, operative, and post-operative ophthalmology notes if crosslinking performed to include:
  - a. All requirements listed above.
  - b. Preoperative corneal pachymetry.
  - c. Cycloplegic refraction and dilated fundus exam.
  - d. Two post-op refractions at least 2 weeks apart that shows stability (no more than 0.50 diopter shift in **manifest sphere**).
  - e. Keratometry readings pre and post-surgery.
  - 7 Slit lamp exam which must include grading of haze, if present. RILO/MEB results, if member demonstrates progression, requires long term treatment, surgical intervention (to include corneal collagen crosslinking), or results in spectacle corrected visual acuity below the level specified in item MSD C2.
  - 8 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1 An interval AMS with particular attention to clinical changes and disease stability.
- 2 Interval eye exam results to include:
  - a. Manifest Refraction Slit Lamp Exam
  - b. Corneal Topography (with parameters as above)
  - c. Slit Lamp Exam
  - d. Pentacam (if available).

## **III. Aeromedical Concerns**

Keratoconics frequently have poor quality of vision. Optical correction mitigates those effects somewhat, but many cases eventually require hard contact lenses to optimize correction. These contact lens fittings, however, are complicated and not always successful. Blurred vision, distorted images, decreased contrast sensitivity, degradation in stereopsis, monocular diplopia, and optical side effects caused by KCN are undesirable and detrimental to flight safety. It is imperative that aircrew carry a set of backup spectacles (and backup contacts if used) on all missions in the event problems arise with contacts making removal necessary.

In addition, corneal hydrops is a known complication in approximately 2-3% of KCN patients. Corneal hydrops is the development of acute and significant corneal edema following a break in Descemet's membrane and endothelium, producing corneal clouding and vision loss. This complication typically only occurs in severe cases of KCN but would be a significant event if it occurred during operations. However, the risk of simultaneous bilateral corneal hydrops is considered to be low and is aeromedically acceptable. Fortunately, hydrops has rarely been observed within the USAF flying population. This may be due to the fact that hydrops is typically associated with younger patients who develop a severe form of KCN that presents at an early age. These individuals would likely be aware of their impaired visual condition and self-select out of an occupation with strict vision requirements. Additionally, as described above, the aeromedical risks of CXL specifically include loss of best corrected vision, treatment failure (progression despite treatment), and corneal haze. However, treating earlier in the disease process and proper patient selection can greatly reduce these risks.

| ICD 9 code for keratoconus                  |  |  |
|---|--|--|
| 371.6                                       | Keratoconus  |  |
| ICD-10 code for keratoconus                 |  |  |
| H18.609                                     | Keratoconus, unspecified, unspecified eye            |  |
| ICD-10 code for abnormal corneal topography |  |  |
| H18.899                                     | Other specified disorders of cornea, unspecified eye |  |

# IV. Suggested Readings

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#### WAIVER GUIDE

Updated: Oct 2017

Supersedes Waiver Guide of: Aug 2013

By: Lt Col Robert Woolley (RAM 18) and Dr Dan Van Syoc

Reviewed by Lt Col John Baron, AF/SG consultant for nephrology

### **CONDITION:**

**Kidney Disease, Chronic (Oct 2017)** 

#### I. Waiver Consideration.

All forms of chronic kidney diseases are disqualifying for aviation duty in the Air Force. The only medications considered for waiver are those on the approved medication list at the time of the waiver submission. After thorough evaluation, the Medical Standards Directory (MSD) and waiver guide should be consulted for conditions such as anemia, diabetes, coronary artery disease, hypertension, electrolyte disturbances and other renal diseases. These conditions may be disqualifying independently or require initial review in lieu of a medical evaluation board (IRILO) through AFPC/DP2NP prior to waiver application. CKD is not specifically disqualifying for ATC and GBO duties; for these personnel, a waiver would only be indicated if they were being treated with an unapproved medication or their condition was sufficiently advanced that their overall health or treatment requirements could impact safety or duty performance, or they required specialty care more frequently than annually.

**Table 1: Waiver potential for Chronic Kidney Disease (CKD)** 

| Flying Class (FC) | Condition     | Waiver Potential                        | ACS                  |
|-------------------|---------------|---|----------------------|
|                   |               | Waiver Authority!                       | Review/Evaluation    |
| I/IA              | Stages 1-5    | No                                      | No                   |
|                   | _             | AETC                                    |                      |
| II*@              | Stages 1-3a   | Yes                                     | If requested by      |
|                   |               | MAJCOM                                  | MAJCOM               |
|                   | Stage 3b & 4  | Maybe                                   | Yes                  |
|                   | Stage 30 to 1 | MAJCOM                                  | 105                  |
|                   |               |   |                      |
|                   | Stage 5       | No                                      | Only if requested by |
|                   |               | MAJCOM                                  | MAJCOM               |
| III*@             | Stages 1-3a   | Yes                                     | No                   |
| SWA               |               | MAJCOM                                  |                      |
|                   | G. 21 0 4     | 3.6.1                                   | 77                   |
|                   | Stage 3b & 4  | Maybe                                   | Yes, if waiver being |
|                   |               | MAJCOM                                  | considered           |
|                   | Stage 5       | No                                      | Only if requested by |
|                   |               | MAJCOM                                  | MAJCOM               |
| ATC/GBO           | Stages 1-3a   | Yes (if required)                       | No                   |
|                   |               | MAJCOM                                  |                      |
|                   |               |   |                      |
|                   | Stage 3b & 4  | Maybe                                   | Yes, if waiver being |
|                   | Stage 30 & 4  | MAJCOM                                  | considered           |
|                   |               | 111111111111111111111111111111111111111 | Completion           |
|                   | Stage 5       | No                                      | Only if requested by |
|                   |               | MAJCOM                                  | waiver authority     |

<sup>\*</sup> No waivers for untrained assets

AIMWTS review in Mar 2017 revealed 27 cases submitted for the diagnosis of chronic kidney disease. There were 0 FCI/IA cases, 8 FC II cases, 3 FC II RPA cases, 13 FC III cases, 1 GBC case, and 1 MOD case. Five of the cases were disqualified; 4 were FC III and 1 was an RPA pilot. Two of the disqualified cases were so dispositioned due to their kidney disease and the other three for a combination of medical conditions.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>@</sup> No indefinite waivers

<sup>!</sup> If CKD requires ongoing specialist care more frequently than annually (and there is a requirement for MEB/I-RILO), then waiver authority as AFMRA.

The AMS for initial waiver for CKD should include the following:

- A. Complete history of the problem to include all consultants seen.
- B. Physical exam results.
- C. Labs Random urine albumin and urine creatinine, random protein and urine creatinine, or 24 hour protein and 24 hour creatinine. Complete urinalysis with microscopic analysis (if heme, nitrate, or leucocyte esterase positive). Serum chemistries to include BMP, calcium, phosphorus, albumin, magnesium and total protein. Calculation of eGFR using MDRD, CKD-epi or calculation of 24hr creatinine clearance based on a 24 hour urine collection (if available). CBC and fasting lipids. Renal biopsy results with complete pathology report (if clinical evaluation of the patient led to a kidney biopsy).
- D. Renal ultrasound (mandatory), any other imaging results (if accomplished).
- E. Nephrologist or internist consultation report.
- F. Current treatment to include all medications and dates started.
- G. Results of MEB (if required) or copy of FL4 from DP2NP.
- H. Detail of all other medical problems, if applicable.

The AMS for <u>waiver renewal</u> for CKD should include the following:

- A. Updated history since last waiver.
- B. Physical exam results.
- C. Labs Urinalysis (ACR if protein positive on dipstick), BMP with albumin and total protein, CBC and lipids at a minimum. Include all other urine studies labs and additional imaging and biopsy results (if applicable) since last waiver.
- D. Most recent nephrologist or internist consultation report.
- E. Current renal treatment to include all medications and dates started.

#### III. Overview.

Chronic kidney disease (CKD) is a worldwide public health problem which claims more lives in the US annually than breast or prostate cancer. The etiology of CKD differs significantly between industrialized and non-industrialized nations, with lifestyle related conditions such as diabetes, hypertension, obesity and cardiovascular disease playing a much greater role in the development of CKD within the US and other "first-world" countries, whereas infectious disease, IgA nephropathy and disorders affecting the urinary outflow tract are much more likely to be the cause in developing nations. For nearly three decades, the incidence and prevalence of CKD has increased in the US, owing to multiple factors including an ageing population, increasing rates of lifestyle related diseases and improved detection through the development and increased clinical use of equations which estimate renal clearance rates. After peaking in 2006, the overall prevalence of CKD in the US has remained fairly stable at around 14%, owing to slight decreases in both incidence and mortality since that time. Renal disease associated with proteinuria, hematuria or congenital anomalies are addressed in other sections of the waiver guide which should be referred to as indicated.

CKD is defined as a moderate reduction in either creatinine clearance or estimated glomerular filtration rate (eGFR) that is persistent for more than 3 months, or the presence of other structural or functional abnormalities such as blood or protein in the urine,

persisting for 3 months or more.<sup>4</sup> The most commonly used method for estimating the glomerular filtration rate (GFR) at present is the Modification of Diet in Renal Disease (MDRD) or Levey equation which typically uses the variables of age, gender, serum creatinine level and race (black vs. non-black) to calculate a result.<sup>4-6</sup> Because body size is correlated with both creatinine levels and clearance rate, the MDRD equation is normalized to a "standard" body surface area of 1.73 m<sup>2</sup>, allowing comparison between individuals of differing body types.

Recently, there are newer equations which have proven to be more accurate when compared with MDRD, especially among those with lesser degrees of renal impairment. Most prominently is the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation which uses the same variables as the MDRD equation but is less commonly reported on laboratory results. CKD-EPI is also normalized to a body surface area of 1.73 m<sup>2</sup>. More accurate still is the CKD-EPI equation that includes the additional variable of a serum cystatin C which is less affected by lean muscle mass than is creatinine. 8

Proteinuria has previously been diagnosed using timed collections for quantification. Several studies have demonstrated the validity of using spot ratios in place of these timed collections for diagnostic purposes, however use of such ratios must be taken in context and may be misleading. Typically a urine protein to creatinine ratio of more than 30 mg/g and protein/creatinine ration greater than 150 is considered evidence of renal disease, however, there are benign disorders which may elicit such a result. Strenuous exercise will almost always be associated with both proteinuria and hematuria and a condition called orthostatic proteinuria (OP) is relatively common among the young but becomes fairly rare in adulthood. OP may be easily diagnosed after an appropriate period of rest by performing a timed collection during which the subject remains in the supine or recumbent position (usually 4 to 8 hours). If proteinuria is absent and there are no other indications of disease such as edema or hypoalbuminemia, one may consider this to be OP. Such cases should be followed with a routine urinalysis each year as OP typically resolves by the 3<sup>rd</sup> decade of life.

An eGFR of less than 60mL/min/1.73 m² of body surface area or an albumin to creatinine ratio (ACR) ≥ 30 mg/g are considered indicative of underlying renal disease.<sup>6</sup> Often referred to as Stage I to Stage V, one need not necessarily progress from one to the next. Mildly reduced clearance in and of itself is not diagnosed as CKD, thus Stage I and II are only diagnosed when there is another indication of structural or functional damage such as the presence of proteinuria. Stage III through V are determined solely based on moderate or greater deficiencies in clearance and may or may not be accompanied by other abnormalities.<sup>3,7</sup> The progression of renal disease is non-linear and mild disease may persist for decades before declining precipitously.<sup>11</sup> Most individuals with CKD will not progress to End Stage Renal Disease (ESRD) which requires dialysis therapy or transplant.<sup>1</sup> More commonly, those with CKD will succumb to other cardiovascular diseases of which the renal disease may be both an etiologic factor and/or an indication of underlying vascular disease from another cause.<sup>2, 12, 13</sup>

Moderate to severe CKD is associated with accumulation of waste products, electrolyte imbalances, anemia, osteodystrophy and potentially problems with volume regulation.<sup>3, 14</sup> These conditions may not become symptomatic until much later in the course of the disease, however, early identification and treatment may effectively reduce or prevent their occurrence. Strategies may also be employed which have the potential for slowing decline in renal function, these include control of hypertension and blood sugar, appropriate weight loss and other novel approaches. Currently, routine screening for renal disease at periodic health examinations is not considered to be of benefit at the population level, however, screening for those in higher risk groups is likely warranted.<sup>7, 15, 16</sup> Highrisk groups include those with conditions previously mentioned such as hypertension, diabetes or cardiovascular disease, as well as those with recurrent urinary tract infections, kidney stones, known anatomic abnormalities or a family history of renal disease.

In general, patients diagnosed with CKD should have renal imaging studies performed as part of their initial evaluation.<sup>17</sup> Typically, renal ultrasonography is readily available and can provide an appropriate amount of information in determining the overall anatomy as well as giving clues to the nature and duration of disease. Further studies may be warranted based on the clinical picture but are often not necessary. If studies involving administration of intravenous contrast material are recommended, it is advisable to consult with a nephrologist before proceeding as both iodine and gadolinium based media have been associated with adverse outcomes in the renally impaired.

Staging of CKD has become a valuable tool in identifying both level of kidney function and establishment of clinical practice guidelines which address the evaluation and treatment of common comorbidities which can occur as renal function declines. Although not universally adopted, many organizations have divided stage III into IIIa and IIIb as it is during this stage that higher risks and several comorbidities may become apparent. Most patients with Stage IIIa CKD without other functional or structural abnormalities can be successfully managed by their primary care physician utilizing published clinical practice guidelines. As mentioned earlier, progression of renal disease is non-linear and function may decline rapidly during the later stages. For this reason, specialty referral is indicated when eGFR drops below the CKD IIIa range or when other indications of renal damage exist.

Management of CKD is well described in the Kidney Disease Outcomes Quality Initiative (KDOOI) guidelines and is not discussed in this waiver guide. <sup>14</sup>

**Table 2: Stages of Chronic Kidney Disease<sup>3</sup>** 

| Stage | Description                        | <b>GFR</b> (mL/min/1.73 m <sup>2</sup> ) |
|-------|------------------------------------|--|
| Ι     | Kidney Damage with normal or ↑ GFR | <u>≥</u> 90                              |
| II    | Kidney Damage with mild ↓ GFR      | 60 - 89                                  |
| IIIa  | Moderate ↓ GFR                     | 45 - 59                                  |
| IIIb  | Moderate ↓ GFR                     | 30 - 44                                  |
| IV    | Severe ↓ GFR                       | 15 - 29                                  |
| V     | Kidney Failure                     | <15 (or dialysis)                        |

Most patients with CKD will die with, not of the renal insufficiency, the majority will succumb to cardiovascular insult and only a very few will progress to end-stage renal disease (ESRD)<sup>2</sup>. Nonetheless, preparation and prevention are essential to reducing future morbidity and mortality. The KDOQI guidelines can be invaluable in assisting the primary care provider with risk management.

Occasionally patients will present with advanced renal disease that is stage IIIb or worse. In those cases specialty referral is indicated, but it is important that care be taken to avoid otherwise normal clinical interventions that may inadvertently preclude future therapy. Blood transfusion should be avoided unless required as a lifesaving measure. Every unit of nonautologous blood has the potential of inducing antibody formation, thereby decreasing the potential of a high quality match for a kidney transplant. Second, is preservation of venous access, should a patient require hemodialysis, damage to superficial and central vessels from venipuncture and other procedures may complicate vascular access creation. The best practice is to limit venipuncture to the dominant extremity, using only the most distal accessible vessels.

## IV. Aeromedical Concerns.

CKD - in its early stages – is associated with a low risk of sudden incapacitation and is generally not associated with sensory or functional impairments in the aviator. The sporadic, non-linear progression of CKD is of far greater concern in this population. Advanced disease is often associated with anemia, perturbations of volume status and electrolyte imbalances, each of which can lead to physiologic incapacitation under the stresses encountered during flight. Additionally, the frequent medical care associated with moderate to severe CKD can come in direct conflict with the mobility requirements of aircrew and special duty operators. Our current inability to predict progression due to the non-linear nature of declining function makes it unwise to train new aviators with even mild degrees of CKD and make waivers inadvisable for that group. Trained aviators and those without responsibility for the primary control of the aircraft, may safely continue their roles until the requirements for medical follow-up, essential medications or comorbid conditions preclude continued service. Maximal therapy aimed at risk modification should be preeminent and should not be postponed or overlooked for the sake of maintaining flying status.

| ICD-9 codes for Chronic Kidney Disease |                                     |  |
|--|-------------------------------------|--|
| 585.1-5                                | Chronic Kidney Disease stages I-V   |  |
| 585.6                                  | End Stage Renal Disease             |  |
| 585.9                                  | Chronic Kidney Disease, unspecified |  |

| ICD-10 codes for Chronic Kidney Disease |  |  |
|---|--|--|
| N18.1-5                                 | Chronic Kidney Disease, stages I-V                     |  |
| N18.6                                   | End Stage Renal Disease                                |  |
| N18.9                                   | Chronic Kidney Disease, unspecified                    |  |
| I18.1                                   | Hypertensive Chronic Kidney Disease, Stage V or ESRD   |  |
| I18.9                                   | Hypertensive Chronic Kidney Disease (all other stages) |  |

## V. References.

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## **Lattice Degeneration (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

**Significant Changes:** LD and low risk atrophic retinal holes with refraction  $\leq$ -5.50 is not disqualifying. Waiver potential for LD and low risk atrophic retinal holes with refraction from -5.75 to -8.00. MSD C42.

## I. Waiver Consideration

Lattice degeneration (LD) is disqualifying for Flying Class I, IA, II, III, and SWA duties when refraction exceeds -5.50. Lattice degeneration is not disqualifying for ATC, GBO, and OSF personnel, nor is it disqualifying for retention purposes. LD is considered high risk if there is a retinal hole present with subretinal fluid or vitreous traction. No waivers are currently being recommended for LD with high-risk characteristics for FC I/IA. The ACS is currently studying the axial length (length of the eye) to determine a better association with lattice degeneration, refractive error, and retinal detachment risk. Current members of the ACS Lattice Degeneration Management Group may be asked to come to the ACS for data collection, but generally, waiver recommendation is made by ACS case review only.

Table 1: Waiver potential for lattice degeneration and low risk atrophic retinal holes

| Flying Class (FC) | Waiver<br>Potential | Waiver Authority | ACS Review or<br>Evaluation |
|-------------------|---------------------|------------------|-----------------------------|
| FC I/IA           | Yes <sup>1</sup>    | AETC             | Yes                         |
| FC II/III         | Yes <sup>1,2</sup>  | MAJCOM           | Yes                         |
| SWA               | Yes <sup>1,2</sup>  | MAJCOM           | MAJCOM                      |
| ATC/GBO/OSF       | N/A                 | N/A              | N/A                         |

<sup>1.</sup> LD and low risk atrophic retinal holes may be waived for FC I/IA, as well as initial FC II, SWA, and FC III, if the member has been evaluated by an ophthalmologist or retinal specialist, who has ruled out the presence of untreated high risk peripheral holes or breaks, retinal traction or sub-retinal fluid, and native refractive error (pre-corneal surgery, if applicable) does not exceed -8.00 diopters. ACS review/evaluation required for initial waivers and at the discretion of the MAJCOM for waiver renewals. LD and low risk atrophic retinal holes with refraction ≤-5.50 are not disqualifying.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

<sup>2.</sup> Waiver for history of retinal detachment is possible if treatment results in stable vision that is within accepted standards.

# A. <u>Initial Waiver Request:</u>

- 1. List and fully discuss all clinical diagnoses requiring a waiver.
- 2. Symptoms, degree of lattice degeneration, degree of myopia (pre-refractive surgery, if applicable), and axial length of both eyes.
- 3. If there is a history of retinal detachment; discuss fully to include all treatments and post-treatment results (visual acuity, visual fields, status of other eye).
- 4. Details of complete ophthalmologic exam, to include presence and location of retinal holes, presence or absence of subretinal fluid, and presence or absence of vitreo-retinal traction.
- 5. Comprehensive ophthalmologist exam (Retinal specialist exam if there is a history of retinal detachment).
- 6. Copies of any photos, if they exist (photograph or digital).
- 7. Medical Evaluation Board results, if applicable.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interim history specifically discussing any recurrences or any changes in the disease pattern and vision status.
- 2 Details of complete ophthalmologic exam.
- 3 Comprehensive ophthalmologist exam to include presence and location of retinal holes, presence or absence of subretinal fluid, and presence or absence of vitreoretinal traction (Retinal specialist exam if there is a history of retinal detachment).
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## **III. Aeromedical Concerns**

Retinal detachment is the primary aeromedical concern. This can result in decreased or loss of vision, visual field changes, abnormal stereopsis, and proliferative vitreoretinopathy. All of these conditions can compromise visual function to such a degree that continued aviation duty is not possible. Detachment is usually sudden and without warning and can be quite incapacitating.

Although LD remains stable in most cases (97%), it can cause, or be associated with RD, especially in higher degrees of myopia. LD is the direct cause of RD in 21% of cases, and is present in 41% of all RD cases. Seventy percent of RD, associated with LD, occurs in patients younger than 40 years of age. LD is more common in myopia; 70% of RD are seen in myopic eyes, with 75% of those RD in myopes with refractive error of -3.00D or greater. The risk of RD in association with any amount of LD increases with the degree of myopia, especially when the refractive error is greater than -5.00D.

In 1989, two major studies were conducted regarding the incidence of retinal detachment in myopic patients with LD. One was a retrospective study observing the characteristics of 176 retinal detachments. Using an annual RD risk of 0.38% and assuming an average lifespan of 79 years, they extrapolated a lifetime RD risk of 35.9% in patients with lattice

degeneration and myopia greater than -5.00, whereas those with lesser myopic refractive errors between -1.00D and -3.00D incurred a 5.3% lifetime RD risk. The other major study at that time observed 423 eyes over 1-25 years (mean 10.8 years) and found three clinical retinal detachments with an overall rate of 0.7%. This translates to a 0.07% annual risk of retinal detachment over the average observed time. This study further followed patients out up to 25 years and no patients had additional clinical retinal detachments. More recently, a study in Japan found a cumulative risk of retinal detachment from atrophic holes at a rate of 1.5% by age 40.

To take the most conservative approach possible, prior waiver recommendations were made on the most concerning statistic available, which was the 35.9% lifetime RD risk. However, this statistic was an estimation and the majority of the retinal detachments occurred at a mean age of 52, which is much older than the typical active duty pilot population. Other studies have subsequently shown a much lower 10-year RD risk ranging from 0-1.4%. To rectify this difference, the ACS has been tracking progression to retinal tears or retinal detachments in aviators with lattice degeneration through the Lattice Degeneration Study Group. While only 4.6 years into the 10 year study, preliminary data shows an annual rate of retinal tears of 0.48% and retinal detachment of 0.08%. This aligns much better with the other studies quoted and supports a much more favorable aeromedical risk profile.

There is no specific treatment for lattice degeneration, but high-risk atrophic holes or breaks can be treated by cryothermy, laser photocoagulation, or diathermy. In an evidence-based analysis of prophylactic treatment of asymptomatic retinal breaks and LD, a panel of vitreoretinal experts reviewed the ophthalmology literature. They concluded that there was insufficient information to strongly support prophylactic treatment of lesions other than symptomatic flap tears. If the condition leads to a retinal detachment, the vast majority can be repaired permanently, allowing the flyer to return to aviation duty due to a lack of increased further risk of retinal detachment.

A theoretical concern with LD is an increased risk of open angle glaucoma, specifically from pigment dispersion. It is recognized that various types of pigmentary disturbances can be seen in up to 80% if LD cases, particularly in cases with high myopia.

Review of AIMWTS data in Sep 2019 revealed 1046 cases since 1 Jan 2014 with a listed diagnosis of lattice degeneration. There were a total of 171 FC I/IA cases (21 disqualified), 372 FC II cases (13 disqualified), 56 RPA pilot cases (11 disqualified), 415 FC III cases (48 disqualified), 8 ATC/GBC cases (0 disqualified) 20 SWA cases (0 disqualified), and 4 MOD cases (1 disqualified).

| ICD-9 codes for Lattice Degeneration |                                  |  |
|--------------------------------------|----------------------------------|--|
| 362.6                                | Peripheral retinal degenerations |  |
| 362.63                               | Lattice degeneration             |  |

| ICD-10 codes for Lattice Degeneration |  |  |
|---------------------------------------|--|--|
| H35.40                                | Unspecified peripheral retinal degenerations   |  |
| H35.411                               | Lattice degeneration of retina, right eye, .412 left eye, .413 bilateral, .419 unspecified |  |

## **IV. Suggested Readings**

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### WAIVER GUIDE

Updated: Jun 2013

Supersedes Waiver Guide of Feb 2009

By: Lt Col Michael Hodges (RAM 13) and Dr. Dan Van Syoc Reviewed by Col Kent McDonald, ACS chief of Neuropsychiatry

## **CONDITION:**

**Learning Disabilities (Jun 2013)** 

### I. Waiver Considerations.

A history of a learning disability is disqualifying for appointment, enlistment and induction into the US Air Force. It is also disqualifying for retention in the military, from an administrative perspective. The MSD lists learning disabilities as disqualifying for all flying classes to include GBO, ATC, and SWA.

**Table 1: Waiver potential for Learning Disabilities** 

| Flying Class (FC)                 | Waiver Potential<br>Waiver Authority | ACS review/evaluation |
|-----------------------------------|--------------------------------------|-----------------------|
| I/IA                              | Maybe<br>AETC                        | Yes <sup>1</sup>      |
| UNTRAINED –<br>II/III/ATC/GBO/SWA | Maybe                                | Yes <sup>1</sup>      |
| TRAINED – II/III and RPA Pilot    | Maybe<br>MAJCOM <sup>2</sup>         | Yes <sup>1</sup>      |
| ATC/GBO/SWA                       | Maybe<br>MAJCOM <sup>2</sup>         | No                    |

<sup>1</sup> ACS review/evaluation if requested by AETC for initial FC I/IA, FC II, and FC III applicants. 2 For untrained FC II, and FC III personnel, as well as ATC/GBO/SWA, waiver authority is AETC,

without any accommodations and there must be no evidence of current problems. Waiver may be considered for aircrew with a history of LD, providing they are symptom free and have not manifested a degradation of their performance of aircrew duties.

AIMWTS review in Feb 2013 for all variations of learning disabilities revealed a total of 14 cases with six resulting in a disqualification disposition. There were a total of 7 FC I/IA cases, one was disqualified. There were no FC II cases. There were a total of 5 FC III cases with 2 disqualified. One member was applying for loadmaster duties and could not pass the Reading Aloud Test which was felt to be secondary to English not being his native language (member inappropriately labeled as LD), while the other case was a flight nurse applicant with dyslexia. Of the 3 ATC cases, all 3 where disqualified for learning difficulties during their apprenticeship.

otherwise it is the MAJCOM of assignment.

For FC I/IA applicants to receive a waiver, their academic record must have been achieved

# II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

AFI 48-123 – Chapter 6 (pg. 55) and the Aeromedical Consultation Service (ACS) Waiver Guide addresses waiver evaluations

Step 1 - Is the aviator ready for waiver submission? A. Waiver is submitted when 1) the member is asymptomatic and 2) medications/psychotherapy treatment have been completed, as applicable to diagnostic category, for the specified time-frame below (Note: psychotherapy "booster sessions", and sometimes SSRIs, are permissible and often advisable after initial symptom resolution): 1 Year—Psychotic Disorders & Somatoform Disorders 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior Discretion of Flight Surgeon—Adjustment Disorders & V-Codes requiring waiver For Traumatic Brain Injury cases, please refer to TBI Waiver Guide For aviators with any other psychiatric disorders, please refer to AFI 48-123 and ACS Waiver Guide B. To be considered for an aeromedical waiver, any disqualifying condition must meet the following criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg. 57-58): Not pose a risk of sudden incapacitation Pose minimal potential for subtle performance decrement, particularly with regard to the higher senses Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment If the possibility of progression or recurrence exists, the first symptoms or signs must be easily detectable and not pose a risk to the individual or the safety of others Cannot require exotic tests, regular invasive procedures, or frequent absences to monitor for stability or progression Must be compatible with the performance of sustained flying operations Step 2 - Before beginning the Aeromedical Summary (AMS), Flight Surgeon must obtain Mental Health consultation and ensure it contains items specified below: Instructions for the Mental Health Provider The mental health evaluation must include a comprehensive written report addressing: Consultation must address each criteria in Step 1B Clinical mental health history (description of symptoms, treatment modality, frequency and compliance with treatment, relevant personal and family history, and perceived impact on occupational duties) Medication history (dates of initial prescription and termination, reason for termination, dosage,

compliance, response, clinical course since termination)

|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile ** for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results **  |
|----------|---|
|          | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental  |
|          | illness) Current and past aviation related duties and any history of current and past occupational  |
|          | performance difficulties (to include perceived impact of mental health condition on performance of duties)  |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep  |
|          | Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended neuropsychological tests. |
|          | Current mental status   |
|          | Diagnosis   |
|          | Motivation to fly or engage in special duty operations (past and current)   |
|          | Recommendation for future psychological and medical treatment   |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
|          | Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand f shipment to ACS Neuropsychiatry Branch   |
| Step 3 - | - Items for the Flight Surgeon to include in the AMS:   |
|          | AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safe   |
|          | Summarize Mental Health history and focus on occupational impact  |
|          | ** If 2 or more months have passed since the comprehensive evaluation/report was completed, the flight surgeon should address how the member has done since and consult with the mental health provider if the member has been seen at mental health since the evaluation**                       |
|          | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)   |
|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile  |
|          | ** for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results ** Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if possible - please address current state of any triggers for the mental illness)                        |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep  |
|          | Current mental status   |
|          | Diagnosis   |
|          | Motivation to fly (past and current)  |
|          | Recommendation for future psychological and medical treatment   |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
|          |   |

Step 4 - Items to complete the waiver package:

| Letter of support from command   |
|--|
| Comprehensive mental health written-report   |
| Confirm mental health has made copies of chart(s) and testing. When requested send to: |
| ACS Aerospace Medicine Branch, USAFSAM/FECA c/o Neuropsychiatry Branch                 |
| 2510 Fifth Street Bldg 840   |
| Wright Patterson AFB, OH 45433-7913  |
| Fax: (937) 904-6296 DSN: 674-9296  |

Please feel free to contact the ACS Neuropsychiatry Branch with questions:

Mr. John Heaton: 798-2766

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for learning disorder should include the following:

- A. AMS detailing any social, occupational, administrative or legal problems, including an analysis of the aeromedical implications of this particular case history.
- B. Mental health evaluation summary, *specifically including* psychological and neuropsychological evaluation reports (with their raw data), and any pertinent past medical or mental health records.
- C. Any pertinent current neurological or other medical consultation reports.
- D. For FC I/IA, detailed history of academic achievement and use of any accommodations.
- E. For trained FC II or III, a letter from the flyer's aviation supervisor or commander supporting a return to flying status.

The AMS for <u>waiver renewal</u> for learning disorder should include the following:

- A. Interval history.
- B. All applicable testing results.
- C. Consultation from mental health professional.

#### III. Overview.

A learning disability is a persistent higher order cognitive deficit that interferes with learning and academic achievement, especially in reading, spelling, writing and/or arithmetic in the context of average or above average intelligence. The term, "learning disability," once associated with reading problems, is often misunderstood, and is a non-specific term for numerous disorders of cognition in various combinations and levels of severity. Such variability leads to a spectrum of aeromedical significance, so that knowledgeable evaluation of the individual and a thorough history on educational achievement, rather than simply identifying the diagnosis, is essential to making a correct aeromedical decision. Previously unrecognized and otherwise irrelevant mild cognitive inefficiencies can prove to be dangerous and result in safety of flight and mission

performance issues in military aviation. Due to problems with overall learning, people identified with learning disabilities as children often suffer from low levels of academic achievement.<sup>2</sup> Since speech and language delays can be a contributing factor in younger ages for learning difficulties, early recognition and intervention is a must.<sup>3</sup> Success in later educational endeavors can be potentially compromised unless the parents and/or school recognize the problem early and provide appropriate remediation.

There are multiple variations of learning disabilities, but there are three widely accepted categories that include reading, mathematics, and written expression. A given individual may have more than one form of learning disability. The first category is reading disorder which is defined as a significant impairment in reading that does not have any demonstrable cause in visual, hearing or physical disorders; is not related to mental retardation, emotional disturbance; nor does it have any environmental, cultural or economic disadvantage.<sup>4</sup> It is estimated that up to one in five children have a significant problem learning to read. Reading disorder is seen in up to 80 percent of school children labeled with a learning disability, or about four percent of the school-age population.<sup>4,8</sup> All children with this disorder share three key symptoms: inaccurate reading, slow reading, and poor reading comprehension. Reading is a totally different skill than oral language. It requires the brain to link written markings to spoken language. To break it down further, the act of reading is actually at least two different processes: basic reading which has to be taught and is letter-sound knowledge along with word recognition, storing and decoding; and reading comprehension, which is the ultimate goal.<sup>4</sup> Dyslexia is the most commonly recognized form of reading disorder. One author defined dyslexia as an unexpected difficulty in reading in children and adults who otherwise possess the intelligence and motivation necessary for accurate and fluent reading.<sup>5</sup> Although the etiology of dyslexia is not known, there are various theories. One is the "Cerebellar Deficit" theory where non-verbal, sensory-motor impairments are felt to have an effect for bringing about dyslexia.<sup>6</sup> Another is the "Phonological Deficit" hypothesis where dyslexia individuals suffer from a deficit in phonological skills where they have a problem reading nonwords. The severity of impairment in individuals with this disorder varies widely. There are numerous models being developed in an effort to identify children at an early age and to intervene in an effective manner.<sup>7,9</sup> Patients with reading disabilities require lifelong assistance, and for secondary and college students, the emphasis is on accommodations, to include extra time, and help with different study skills and test taking.8

The second category of learning disabilities is mathematics disorder which is an impairment of arithmetic or mathematic skills that is sufficiently serious to interfere with academic achievement or daily living. This may affect up to six percent of school age children. The only proven treatment of mathematics disorder is systematic instruction.<sup>4</sup>

The last major category is the disorder of written expression, which some call dysgraphia. It is a significant impairment in written communication that is not attributable to the same issues outlined under reading disorder. It is commonly expressed with spelling, grammatical/syntax or punctuation errors, poor paragraph organization, and excessively

poor handwriting. Most studies to date indicate that individuals with the disorder have persistent problems with written language into late childhood and adolescence.<sup>4</sup>

Until the past couple of decades, little thought was given to adult manifestations of learning disabilities. Clinicians now realize these disorders, once felt to "burn themselves out" in adolescence, can persist into adulthood. Even though it does not disappear, given early intervention and positive educational experiences, many of these people can show a remarkable ability to learn and succeed. Both genetic and environmental factors are undoubtedly important in the etiology of these disorders. Physiological as well as anatomic markers are being sought. Still, current science requires thorough clinical, historical, and, often, psychometric evaluation in order to make these diagnoses. Learning disabilities may be associated with underlying abnormalities in cognitive function, including deficits in attention, memory, or linguistic processes. Impaired vision or hearing may affect learning ability and should be investigated through audiometric or visual screening tests. A learning disability may be diagnosed in the presence of such sensory deficits *only* if the learning difficulties are in excess of those usually associated with these deficits.

#### IV. Aeromedical Concerns.

Typically, significant problems will become manifest in childhood or adolescence and well before an individual is considered as an applicant for aviation service, and the individual will not be selected for flying duties on the basis of low academic performance and/or screening tests (such as the AFOQT). Additionally, it is unlikely that a person with an identified learning disability for which remedial services were provided will be able to successfully complete rigorous military aviation training. As otherwise intelligent officers will have great difficulty keeping up with the rigors of training and operational flying, a confirmed diagnosis of LD is disqualifying for flying class FC I duties, unless the individual can demonstrate passing academic performance off medication and /or solid job performance off medication for a period of no less than 12 months. A history of a learning disorder will not necessarily disqualify a member. Severity and nature of the disorder should be documented. In addition, LD and other psychiatric diagnoses made during childhood are occasionally found to be unsubstantiated in light of a careful, accurate history, and instead can be the result of over-eager achievement-driven parents. This is particularly true if the service member has had no symptoms since early childhood.

| ICD-9 Codes for Learning Disabilities |   |  |
|---------------------------------------|---|--|
| 315.0                                 | Specific Reading Disorder                 |  |
| 315.02                                | Developmental Dyslexia                    |  |
| 315.1                                 | Mathematics Disorder                      |  |
| 315.2                                 | Other Specific Learning Difficulties      |  |
| 315.3                                 | Developmental Speech or Language Disorder |  |
| 784.61                                | Alexia and Dyslexia                       |  |

| ICD-10 Codes for Learning Disabilities |   |  |
|--|---|--|
| F81.0                                  | Specific Reading Disorder                               |  |
| R48.0                                  | Dyslexia and Alexia                                     |  |
| F81.2                                  | Mathematics Disorder                                    |  |
| F81.89                                 | Other Development Disorders of Scholastic Skills        |  |
| F81.9                                  | Development Disorders of Scholastic Skills, Unspecified |  |

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### WAIVER GUIDE

Updated: May 2017

Supersedes Waiver Guide of Dec 2013

By: Lt Col Robert McCoy (RAM 18) and Dr. Dan Van Syoc

Reviewed by Dr. Edwin Palileo & Lt Col Eddie Davenport (Chief Cardiologist ACS)

## **CONDITION:**

Left Bundle Branch Block (May 2017)

### I. Waiver Consideration.

Left Bundle Branch Block (LBBB) is disqualifying for all classes of flying duties, to include ATC, GBO and SWA duties. It may be waiver eligible for any class of unrestricted flying duties after evaluation. All flyer cases that are being considered for a waiver MUST be seen at the Aeromedical Consultation Service (ACS). Angiography is preferably done during the ACS evaluation. If coronary angiography is normal, waiver is usually recommended for unrestricted flying duties. If angiography is abnormal, waiver status will be determined primarily by the extent of CAD and the CAD waiver policy. Reevaluations for LBBB without CAD are typically at three-year intervals and are primarily to follow for the possible development of cardiomyopathy.

Table 1: Waiver potential for Left Bundle Branch Block

| Flying Class (FC) | Waiver Potential<br>Waiver Authority | ACS Review/Evaluation |
|-------------------|--------------------------------------|-----------------------|
| I/IA              | Yes                                  | Yes                   |
|                   | AETC                                 |                       |
| II/III            | Yes                                  | Yes                   |
|                   | MAJCOM                               |                       |
| ATC/GBO/SWA       | Yes                                  | Yes                   |
|                   | MAJCOM                               |                       |

AIMWTS search in Jan 2017 revealed a total of 72 cases carrying the diagnosis of LBBB with 8 total disqualifications. Breakdown of the cases was as follows: 8 FC I/IA cases (1 disqualified), 40 FC II cases (4 disqualified), 23 FC III cases (3 disqualified), and 1 ATC/GBC case. Of the disqualified cases, only two were disqualified for a cardiac reason; one for cardiomyopathy and the other for valvular disease.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. All aircrew with LBBB require ACS evaluation prior to waiver consideration.

The AMS for the <u>initial waiver</u> for LBBB should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. History of symptoms along with a good time line of events.
- C. List all treatments (medications if any) attempted with response.
- D. Original copy of the 12-lead ECG or other ECG tracing documenting LBBB.
- E. Reports of any local consultations.
- F. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. electrocardiogram, treadmill, stress nuclear imaging).

The AMS for waiver renewal for LBBB should include the following:

- A. Interim history since last waiver submission to include symptoms.
- B. Treatments current medications for the condition, if any.
- C. Recent 12-lead ECG.
- D. Reports of any local consultations.

## III. Overview.

LBBB is a pattern seen on electrocardiogram (ECG) when there is delayed conduction throughout the ventricles with characteristic ECG appearance. The normal heart's electrical impulse originates in the sinus node, spreads across the atria, and travels through the atrioventricular node. The impulse penetrates into the ventricles via the His bundle where it then enters the two bundle branches. Soon after, the right and left bundle branches transmit the electrical impulse to the right and left ventricle, respectively. This entire process of ventricular depolarization is completed within about 100 msec, and thus the normal width of the QRS complex is less than 100 msec. In a normally functioning heart, the ventricles contract nearly simultaneously. LBBB usually reflects intrinsic intraventricular impairment of conduction in the left bundle system. The electrical impulse is transmitted through the right bundle branch and myocardium normally while activation of the left ventricle is delayed primarily within the myocardium and occurs after most of the right ventricle has been activated. The impairment can be chronic or transient. It may also appear only when the heart rate exceeds some critical value (rate- or acceleration-dependent LBBB) likely secondary to imbalance in the refractory periods between the two bundle branches. A much less common type is bradycardia-dependent LBBB, in which LBBB occurs only at low heart rates; the responsible mechanism for this seemingly paradoxical situation is not known.<sup>2</sup> Careful examination of the QRS complex and axis (or expert consultation) should be made as an accessory pathway with aberrant ventricular conduction (not a LBBB) can cause a widened QRS complex occurring only at lower heart rates.

The total time for left ventricular depolarization is prolonged with LBBB and leads to prolongation of the QRS interval and sometimes to alterations in the QRS vector. The ECG patterns most commonly seen in LBBB are the characteristic monophasic R wave in I, aVL, and V6 (sometimes M-shaped), and QS (sometimes W-shaped) QRS complex in lead  $V_1$ .<sup>4</sup> The degree of prolongation depends upon the severity of the impairment.<sup>3</sup> A QRS interval greater than or equal to 120 msec is considered a complete LBBB while incomplete LBBB has a shorter 100-120 msec interval.

Unlike right bundle branch block, LBBB is more often a sign of organic heart disease. LBBB is often a marker of one of four underlying conditions: advanced coronary heart disease, long-standing hypertension (with or without left ventricular hypertrophy), aortic valve disease, or cardiomyopathy. More than one contributing factor may be identified. In military aviators we found 10% of those with LBBB had significant CAD on coronary angiography, 2% had dilated cardiomyopathy, and 1% required permanent pacemaker. Over 16 years of follow-up, another 8.5% developed CAD, and 5% developed cardiomyopathy with no additional pacemaker requirements. This increased risk of CAD was also seen in The Women's Health Initiative which followed women with asymptomatic LBBB over a fourteen year time span and showed a hazard ratio of CHD death of 1.43 (95% confidence interval 1.11 to 1.83, p<0.01). In a report from the HOPE trial looking at patients with LBBB over a 4.5 year time period, patients with LBBB compared to those without LBBB, were older, had higher systolic blood pressure and were more likely to be female. Thus LBBB is an important clinical consideration as it may be the first clue to previously undiagnosed, but clinically important abnormalities.

The incidence of LBBB increases with age. <sup>7</sup> It has been reported in 0.01%-0.1% of healthy military aviators versus 0.2%-0.7% of various civilian populations, increasing to over 2% of those over age 75 and over 5% prevalence over age 80 suggestive of a degenerative disease of the conduction system. <sup>8,9</sup> In the non-aviator population, there was an incidence rate of 7/1000 in men and women developing a LBBB before the age of 60. <sup>10</sup> Rate- or acceleration-dependent LBBB has also been shown to be associated with a greater degree of underlying coronary artery disease. <sup>11</sup>

## IV. Aeromedical Concerns.

The prognosis of isolated LBBB in young men is generally benign. 12 Traditionally, there have been two major aeromedical concerns for LBBB. First, does LBBB increase the risk for progressive conduction system disease? And second, is LBBB predictive of current or future underlying cardiac disease? The risk of progressive conduction system disease for newly diagnosed LBBB has not been shown to be increased in otherwise apparently healthy young males.<sup>13</sup> However, acquired LBBB may be the result of advanced and advancing coronary artery disease (CAD).<sup>14</sup> A study in 2012 demonstrated that adjusted mortality rates for patients with new onset LBBB were similar to patients with STsegment elevation myocardial infarction.<sup>15</sup> In the USAF male aviator population aged 35-55 years, estimated background prevalence of significant CAD is about half that of those with LBBB (5% vs. 10%). Thus LBBB has a two-fold increase in risk of underlying significant CAD. Many studies have shown increased major adverse cardiovascular event and increased mortality when LBBB is accompanied by any structural heart disease, congestive heart failure, or coronary artery disease. Thus echocardiography and an ischemic evaluation is absolutely necessary for all cases of LBBB. However, considering the possibility of underlying coronary heart disease and the inaccuracy of many noninvasive tests in the presence of LBBB, invasive coronary angiography might be warranted for definitive diagnosis, especially in older or high-risk aviators. <sup>16</sup> Noninvasive coronary angiography (i.e. CT coronary angiography) is aeromedically acceptable to

exclude coronary heart disease for age under 35 as the risk of significant CAD in this population is well less than 5%. In the absence of underlying cardiac disease, return to unrestricted flying is acceptable. Finally, more recent data suggests there may be structural and functional changes in contractility with increased ventricular dyssynchrony as seen in LBBB and therefore even without CAD or valvular disease, echocardiography at regular intervals is recommended to ensure absence of cardiomyopathy.

| ICD-9 code for Left Bundle Branch Block |                          |
|---|--------------------------|
| 426.3                                   | Left bundle branch block |

| ICD-10 code for Left Bundle Branch Block    |  |  |
|---|--|--|
| I44.7 Left bundle branch block, unspecified |  |  |

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### **WAIVER GUIDE**

Updated: Nov 2016

Supersedes Waiver Guide of Feb 2013

By: Capt Daniel Opris, Dr. Chris Keirns and Lt Col Dara Regn (all from ACS Internal

Medicine branch) and Dr Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

## **CONDITION:**

Leukemia (Nov 2016)

### I. Waiver Consideration.

A history of leukemia is disqualifying for all classes of flying as well as ATC/GBO and SWA duties. The disease is also disqualifying for retention and requires an MEB. Waiver consideration should be delayed until at least one year following completion of active treatment. The patient must be asymptomatic and in remission off all therapies. Due to the heterogeneity of disease and the multitude of factors affecting prognosis and risk, waivers are evaluated on a case-by-case basis by the ACS. Waiver is unlikely to be granted following allogeneic bone marrow transplant, but ACS case review/evaluation is still recommended.

Table 1: Waiver potential for Leukemia.

| Flying Class  | Condition    | Waiver Potential | ACS review/evaluation |
|---------------|--------------|------------------|-----------------------|
| (FC)          |              | Waiver Authority |                       |
| I/IA          | All forms of | Yes#†            | Yes                   |
|               | Leukemia     | AETC\$           |                       |
| II, III, SWA, | All forms of | Yes+*†           | Yes                   |
| ATC, GBO      | Leukemia     | AFMRA\$          |                       |

<sup>#</sup> For FC I/IA individual waiver may be considered after 5 years of remission, asymptomatic.

AIMWTS review in Sep 2016 revealed a total of 33 cases. Seven cases were disqualified (1 FC I, 4 FC II, 1 FC III, and 1 MOD) and 26 were approved for waivers. Six of the seven disqualified cases were primarily disqualified due to the leukemia diagnosis or issues related to the diagnosis. The other case was disqualified for anthropometric reasons.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current

<sup>+</sup> For trained FC II, FC III, SWA, ATC, GBO personnel, waiver may be considered 12 months after treatment completion if asymptomatic with confirmed remission.

<sup>\*</sup> For untrained FC II, FC III, ATC, GBO, and SWA personnel, waiver may be considered after 5 years of remission.

<sup>†</sup> No indefinite waivers

<sup>\$</sup> All initial waivers requests will be routed to AFMRA.

clinical guidelines/recommendations. Ensure that the MEB has been completed prior to submitting the waiver.

The AMS for an <u>initial waiver</u> for leukemia should include the following:

- A. History symptoms, pathology, stage, treatment, including date of last treatment, surveillance plan and activity level.
- B. Physical exam focus on CNS, skin, abdominal and chest exams.
- C. Hematology/oncology consults to include the six month and twelve month follow-ups all consistent with National Comprehensive Cancer Network (NCCN) guidelines for the specific type of leukemia. Also recommended is an objective assessment by the oncologist of the ongoing complications of therapy, evidence of recurrence and recommendations for follow-up.
- D. Labs all with dates, including bone marrow biopsy.
- E. Imaging studies, if obtained.
- F. In patients who received prophylactic CNS radiation, a neurology and psychology review is necessary.
- G. Tumor board report, military or civilian, if applicable.
- H. Medical evaluation board (MEB) disposition.

The AMS for a <u>waiver renewal</u> for leukemia should include the following:

- A. History interim history since last waiver request to include any recent or planned therapy.
- B. Physical exam see above physical exam elements.
- C. Hematology/oncology consults.
- D. Labs all test results since previous waiver.
- E. Imaging studies since last waiver, if done.

### III. Overview.

The leukemias are a diverse set of neoplastic disorders resulting from mutations resulting in malignant transformation of hematologic cells that are classified according to morphological, immunophenotypic, cytogenetic and molecular features. Malignant transformation results in a single mutant hematopoietic progenitor cell that has lost the ability to inhibit proliferation, and is resistant to apoptosis, thereby resulting in malignant, poorly differentiated hematopoietic precursors.<sup>1</sup>

All blood cells (Red Blood Cells (RBCs), Platelets and White Blood Cells (WBCs)) are derived from stem cells and are further separated into two pathways, myeloid or lymphoid. Myeloid stem cells can produce RBCs, platelets or myeloblasts, which are the precursors to granulocytes. Lymphoid stem cells can produce non-granulocyte WBCs. In a person with leukemia, the bone marrow produces abnormal WBCs called leukemia cells and leukemic blast cells. As leukemia cells are resistant to apoptosis, the result is a build-up and crowding out of normal blood cells. This can result in secondary anemia, thrombocytopenia or granulocytopenia.<sup>1,2</sup> Leukemias are divided into myelogenous or lymphocytic based on the origin of the precursor cell. Myelogenous leukemia, also called myelocytic leukemia, arises from granulocytes or monocytes and lymphocytic leukemia

arises from lymphocytes. Each type is further divided into acute or chronic forms of disease.

### **ACUTE LEUKEMIAS**

The clinical presentation of acute leukemia stems from blast cell infiltration of bone marrow or extramedullary sites. As a result, initial symptoms may be due to the presence of anemia, neutropenia, or thrombocytopenia. Nonspecific complaints including weakness, lethargy, fatigue, dyspnea, fever, weight loss, or bleeding may be the first presenting signs of disease. Hepatosplenomegaly or adenopathy may also result from blast cell infiltration of organs or lymph nodes. Bone marrow infiltration can result in bone pain. Mucosal bleeding, petechiae, ecchymosis, and fundal hemorrhages may occur as a result of thrombocytopenia.<sup>1, 2</sup>

## Acute Myelogenous (Myeloid, Myelocytic) Leukemia (AML)

AML is a hematopoietic malignancy leading to the infiltration of blast cells in the marrow and the decreased production of normal blood cells; consequently, anemia, neutropenia and thrombocytopenia develop. AML is the most common acute form of leukemia in adults. It represents 35% of all leukemias in the US and is responsible for about 20% of acute leukemia in children and 80% of adult acute leukemia cases. The median age of adults at diagnosis is 65 and the male:female ratio is nearly 5:3.<sup>3,4</sup> There are numerous predisposing factors in the development of AML, including genetic abnormalities, environmental factors, and other hematologic diseases, but most patients have no significant exposure.<sup>1,3,5</sup>

Clinical manifestations of AML result either from the proliferation of leukemic cells or from bone marrow failure that leads to decrease in normal cells (complications of pancytopenia). Common symptoms include weakness, fatigue, pallor, infections, palpitations, dyspnea on exertion, bleeding tendency, and bone pain. Blasts may infiltrate organs or lymph nodes, resulting in adenopathy or hepatosplenomegaly. Palpable splenomegaly and hepatomegaly occur in about one third of patients, with testicular infiltration being less common. Definitive diagnosis of AML typically requires bone marrow aspiration and biopsy.<sup>5,7</sup>

Treatment with induction therapy includes agents such as daunorubicin, cytarabine, idarubicin and mitoxantrone.<sup>5, 6</sup> Post-induction treatment utilizes allogeneic/autologous bone marrow transplantation or the use of the consolidation chemotherapy after remission is achieved.<sup>5</sup> Central nervous system involvement (meningeal) occurs in 2% of cases at the time of presentation. In these cases, CNS treatment is recommended; high-dose or intrathecal therapy is more commonly used than cranial radiation due to less toxicity.<sup>2</sup> Remission is the more accepted term with AML rather than cure and the remission rates have improved dramatically, but remission, 5-year survival, and cure rates are most dependent on the patient's age and cytogenetic/chromosomal findings when AML occurs.<sup>2</sup>

## Acute lymphoblastic leukemia (ALL)

ALL is a malignant condition that is characterized by lymphoblast (from either B or T cell lineage) proliferation in the bone marrow and extramedullary sites or "sanctuaries", such as meninges.<sup>2</sup> ALL is the most common cancer in children younger than 15 years of age; it occurs mainly in children but any age can be affected. There are many subtypes of this form of leukemia. It represents 12% of all leukemias and 20% of adult leukemias. Males are more commonly affected than females. In most age groups, the incidence of ALL is higher in those of European descent than in those of African descent. Cure rates are 80% for children and less than 40% for adults. The majority of adults treated for ALL with current regimens will relapse.<sup>7,8</sup> The disease can lead to anemia, thrombocytopenia, and neutropenia.<sup>2</sup> No specific cause can be identified in most cases, but there is increased risk associated with patients who underwent antineoplastic treatment or those exposed to ionizing radiation and toxins.<sup>5</sup>

Treatment consists of induction therapy, central nervous system-directed treatment or prophylaxis, and consolidation or maintenance therapy. Induction chemotherapy may include glucocorticoids, conventional chemotherapy, and/or targeted therapy. The central nervous system (CNS) may be a site for relapse as it commonly serves as a sanctuary for leukemic cells. To prevent relapse from a CNS source, treatment targeting the CNS is indicated with the use of systemic and intra-thecal chemotherapy or cranial irradiation. Consolidation or maintenance therapy may include conventional chemotherapy or high dose chemotherapy followed by bone marrow transplantation of an allograft from a matched sibling.<sup>2, 5</sup> In those patients treated with prophylactic CNS radiation as a child, there is concern about the lifetime risk of neurocognitive difficulties, a second cancer and endocrinopathies, as well as problems with bleeding from intracranial vessels. The approach currently has shifted to a more aggressive intrathecal and systemic chemotherapeutic regimen for CNS therapy.

# **CHRONIC LEUKEMIAS**

Patients with chronic leukemia may have a wide range of physical symptoms and laboratory abnormalities at the time of diagnosis. Due to the progressive accumulation of mature and maturing hematologic cells from dysregulated production and uncontrolled proliferation, the overall infiltrative nature of these diseases can cause lymphadenopathy or organomegaly, to B type symptoms (weight loss, fevers, night sweats, fatigue) or a blast crisis, conditions resembling acute leukemia in which myeloid or lymphoid blasts proliferate in an uncontrolled manner. An important consideration is the large percentage of patients that are asymptomatic at the time of diagnosis (20-50% for CML), with the disease process being considered following evaluation of routine blood tests with incidental findings.

# **Chronic lymphocytic leukemia (CLL)**

CLL is a malignant proliferation of small mature looking B-lymphocytes in the vascular and lymphatic systems, as well as in the bone marrow. CLL is considered to be identical to the mature B cell neoplasm small lymphocytic lymphoma (one disease with different manifestations). CLL is the most common adult leukemia in the western world. In the U.S., male incidence is almost twice that of females, and it comprises 30% of all leukemias. The risk increases with age, occurring mostly in the middle-aged and elderly with a median age of onset of 70 years. It is a disease of unknown etiology with a long clinical course.

Patients may present with a wide range of symptoms, signs, and laboratory abnormalities when diagnosed with CLL. Symptoms may range from no symptoms to persistent lymphadenopathy, unintentional weight loss, fevers with or without infection, night sweats, and extreme fatigue. Signs of CLL include lymphadenopathy, splenomegaly, hepatomegaly, and skin lesions (leukemia cutis). Laboratory findings show typical lymphocytosis in the peripheral blood and bone marrow, mild to moderate cytopenia of all cell lines, and less commonly, hypogammaglobulinemia.<sup>9</sup>

Not all patients with CLL require immediate treatment due to the variable survival rates based on the disease subset, lack of scientific evidence of improved survivability with early treatment, and a low cure rate with current treatment regimens (except possibly for allogeneic hematopoietic cell transplantation). The current recommendation during the asymptomatic phase of CLL, based on several prospective randomized trials, is to observe and not treat. Immediate treatment is recommended for patients with advanced disease, high tumor burden, severe symptoms, or repeated infections. There is no standardized treatment for CLL although there are several options. Choice of treatment regimen is determined by patient characteristics and treatment goals. Overall survival rates vary with the treatment regimen.<sup>11</sup>

## Chronic myelogenous (myelocytic, myelogenous, granulocytic) leukemia (CML)

CML is an acquired malignant disorder that is associated with the presence of the Philadelphia chromosome. It commonly results in anemia, granulocytosis, immature granulocytosis, basophilia, thrombocytosis and splenomegaly. CML comprises 15-20% of all adult leukemia cases, with a slightly higher incidence in males compared to females. The median age at presentation is 53. Exposure to high doses of ionizing radiation is known to be the major risk factor and genetic mutations may be a predisposing factor.<sup>12</sup>

Clinical manifestations of CML depend on the phase of the disease at the time of diagnosis: chronic phase, accelerated phase, or blast crisis. Approximately 20-50% of patients are asymptomatic at the time of diagnosis and clues to the disease are found in the peripheral blood. Symptoms, when present, include fatigue, malaise, weight loss, excessive sweating, bleeding tendency, and abdominal fullness. Laboratory findings in CML include white blood cell counts that can rise to the 100,000 micro/L range with predominance of the neutrophilic cell line. Bone marrow aspiration and biopsy show

granulocytic hyperplasia with features consistent with the peripheral blood. Ninety to 95% of CML patients have evidence of the Philadelphia chromosome. The remainder have the BCR-ABL fusion gene, or its product, BCR-ABL fusion mRNA. Several other medical conditions may mimic CML and must be differentiated to determine the appropriate treatment and prognosis. The strongest predictor of prognosis is the stage at which CML is diagnosed: the chronic phase has a much better prognosis compared to the acute phase or blast crisis. <sup>10</sup>

Treatment options include potential cure with allogeneic bone marrow transplant, disease control with tyrosine kinase inhibitors (TKI), and palliative therapy with cytotoxic agents. The treatment of choice for the majority of patients in the chronic phase of CML is a TKI, such as imatinib mesylate. Approximately 8% of patients in the chronic phase are either resistant or intolerant to treatment with imatinib mesylate. Monitoring of residual disease after treatment is a key component in managing patients with CML. <sup>12, 13</sup> The prognosis for these patients has dramatically improved with TKI use and some studies suggest ageadjusted mortality rates similar to the general population.

## **OTHER LEUKEMIA SUBTYPES:**

# Hairy cell leukemia

Hairy cell leukemia is an uncommon neoplastic proliferation of B lymphocytic cells that is similar to CLL but the cell has larger cytoplasm with "hairy projections". It represents 2% of all leukemias. It is now considered to be an indolent non-Hodgkin lymphoma. Its prevalence is higher in males with a male to female ratio of 4:1 with a median age of 52. It is three times more prevalent in Caucasians than African-Americans. Predisposing factors are not completely understood, but possible causes include exposure to ionizing radiation, Epstein-Barr virus, and organic chemicals.<sup>14</sup>

Patients with hairy cell leukemia may be asymptomatic or present in various ways including splenomegaly, pallor, ecchymosis, weakness, fatigue, or infections. Diagnostic tests may show a characteristic peripheral blood smear with "hairy cells" (usually < 20% of circulating white cells), hyper or hypo cellularity of the bone marrow (the latter causing fibrosis), and pancytopenia. Asymptomatic individuals do not require immediate treatment and can often be observed. Treatment is initiated when they become symptomatic. The first-line treatment option is cytotoxic chemotherapy with purine analogs such as cladribine (2-CdA) and pentostatin. Other treatment options include splenectomy and interferon. Life expectancy has greatly improved with this disease; newer therapies have led to overall survival rates greater than 95% at four years.

#### IV. Aeromedical Concerns.

ALL or AML are the most commonly encountered leukemias seen in our active duty aviation personnel. Symptoms of acute leukemia include fatigue, lethargy and malaise and can be associated with infections, anemia and/or hemorrhage (cerebral). Other signs and symptoms may develop as the disease progresses and affects other parts of the body,

such as abdominal discomfort due to splenomegaly. Although rare, patients may even require splenectomy secondary to complications of splenomegaly (spontaneous splenic rupture) which would then present an aviator with an added risk for future development of an overwhelming infection. Disseminated intravascular coagulation is also a common complication of ALL as well as a sub-set of AML and has the potential for causing incapacitating thrombotic and hemorrhagic events. Of note, leukemic involvement of the central nervous system (CNS) at the time of diagnosis is an uncommon finding in AML and ALL. However, CNS preventive therapy with craniospinal radiotherapy or intrathecal chemotherapy may be incorporated into a patient's treatment protocol, particularly for ALL patients. As described above in the ALL subsection overview, CNS radiation has been associated with a number of aeromedically significant long-term complications.

Treatment regimens, both chemotherapeutic and CNS irradiation, for virtually all types of leukemia can have a multitude of side effects and complications that degrade performance and safety; in general, radiation therapy has a limited role in the treatment of most forms of leukemia.<sup>17</sup> Importantly, active leukemia of any type or ongoing therapy is not compatible with flying duties and will not be considered for a waiver.

| ICD-9 codes for leukemia |                              |  |
|--------------------------|------------------------------|--|
| 204-208 (range)          | All leukemias                |  |
| 204                      | Lymphoid leukemias           |  |
| 205                      | Myeloid leukemias            |  |
| 206                      | Monocytic leukemias          |  |
| 207                      | Other specified leukemias    |  |
| 208                      | Leukemia NOS                 |  |
| 204.0                    | Acute lymphoblastic leukemia |  |
| 205.0                    | Acute myelogenous leukemia   |  |
| 204.1                    | Chronic lymphocytic leukemia |  |
| 201.1                    | Chronic myelogenous leukemia |  |
| 202.4                    | Hairy cell leukemia          |  |

| ICD-10 codes for leukemia |  |  |
|---------------------------|--|--|
| C91.91                    | Lymphoid leukemia, unspecified, in     |  |
|                           | remission                              |  |
| C92.91                    | Myeloid leukemia, unspecified, in      |  |
|                           | remission                              |  |
| C93.91                    | Monocytic leukemia, unspecified, in    |  |
|                           | remission                              |  |
| C94.81                    | Other specific leukemias, in remission |  |
| C95.91                    | Leukemia, unspecified, in remission    |  |
| C91.11                    | Chronic lymphocytic leukemia of B-     |  |
|                           | cell type in remission                 |  |
| C92.11                    | Chronic myeloid leukemia,              |  |
|                           | BCR/ABL-positive, in remission         |  |
| C91.41                    | Hairy cell leukemia, in remission      |  |

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### **WAIVER GUIDE**

Updated: May 2014

Supersedes Waiver Guide of Aug 2010

By: Lt Col Niraj Govil (RAM XV) and Dr. Dan Van Syoc Reviewed by Col Pat Storms, RAM and gastroenterologist

# **CONDITION:**

Liver Function Testing (Transaminases) and Gilbert's Syndrome (May 2014)

## I. Waiver Consideration.

Chronic liver disease is disqualifying for all flying classes including ATC/GBO or SWA personnel. For abnormal liver function tests, waiver consideration will hinge on the specific diagnosis and the functional hepatic capacity, as described above. The specific disqualifying diagnoses should be the focus of waiver package preparation. The initial waiver request should address, in a comprehensive manner, the diagnostic testing resulting either in a specific diagnosis, or the exclusion of other diseases to result in a diagnosis of "abnormal liver function tests of unclear etiology". Re-evaluation requests should focus on any new testing that could reveal a diagnosis not previously made (if appropriate), or that testing which demonstrates stability of hepatic function over time. Congenital hyperbilirubinemia diseases, i.e. Gilbert's, are not disqualifying if the patient is asymptomatic; no waiver is required. If an individual has Gilbert's syndrome with symptoms then a waiver would be required and an internal medicine or gastroenterology consult is recommended.

Table 1: Waiver potential for abnormal liver function tests and Gilbert's Syndrome

| Flying Class (FC) | Condition        | Waiver Potential |
|-------------------|------------------|------------------|
|                   |                  | Waiver Authority |
| I/IA              | Liver Impairment | Yes              |
|                   |                  | AETC             |
| II*               | Liver Impairment | Yes              |
| III*              |                  | MAJCOM*          |
| ATC/GBO/SWA       |                  |                  |

<sup>\*</sup> AETC is waiver authority for initial certification for FC II and FC III

AIMWTS review in February 2014 resulted in 34 aviators with a waiver submitted for liver disease that included abnormal liver functions tests; 5 of these cases resulted in a disqualification disposition, none of which were attributable to the abnormal lab tests. There were 12 additional aviators with a waiver submitted for Gilbert's syndrome; 2 were disqualified for diagnoses other than the Gilbert's.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for liver disease with abnormal liver function tests should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of any diagnosed liver disease and abnormal liver function testing to include any family history of liver diseases.
- C. Labs: all liver function test results, CBC, hepatitis profile. For Gilbert's, also need a reticulocyte count, as well as unconjugated and conjugated bilirubin levels.
- D. Imaging: all results of any performed imaging tests.
- E. Consultation from a gastroenterologist or internal medicine specialist.

The AMS for <u>waiver renewal</u> for liver disease with abnormal liver function tests should include the following:

- A. Interval history from past waiver request with any pertinent updated information.
- B. All applicable labs and imaging tests as in the initial aeromedical summary.
- C. Consultation from a gastroenterologist or internal medicine specialist.

## III. Overview.

Liver function tests are the markers of diseases that may have aeromedical implications. Abnormal liver function tests alone are not disqualifying, but the diseases that manifest the abnormal tests may well be. The following topics in the AF Medical Standards Directory (MSD) relate specifically to liver disease: history of viral hepatitis, with carrier state, persistent aminotransferase (previously termed "transaminase") elevation or evidence of chronic active or persistent hepatitis, marked enlargement of the liver from any cause including hepatic cysts. Drugs are a relatively common cause of liver insult, which usually is recognized as abnormalities seen with serum liver testing. At least 300 agents have been implicated in drug-induced liver injury. In addition, among tens of thousands of chemical compounds in commercial and industrial use, several hundred are listed as causing liver injury by the National Institute for Occupational Safety and Health (NIOSH), as published in their most recent Pocket Guide to Chemical Hazards.<sup>2</sup>

Aminotransferases (AST/ALT) and gamma glutamyl transpeptidase (GGT) are sensitive indicators of hepatocellular injury due to their abundance in hepatocytes. Normal range is generally 30-40 U per liter, but varies widely among laboratories. They are released into the bloodstream in increasing amounts when the liver cell membrane is damaged. Most common causes of elevated aminotransferase levels are: alcohol, chronic viral hepatitis, autoimmune hepatitis, hepatic steatosis and steatohepatitis, hemochromatosis, toxins, drugs, ischemia, Wilson's disease, alpha-1 antitrypsin deficiency, and (more recently recognized) celiac sprue. An AST to ALT ratio of > 2:1 should raise concern about alcohol injury. With a ratio of 3:1, 96% of patients in one study were confirmed to have alcoholic liver disease.<sup>3</sup> Ratios of AST/ALT of > 5, particularly if the ALT is normal or only slightly elevated, may be seen in rhabdomyolysis or strenuous exercise, a situation that may well be encountered in a military training or deployed environment.<sup>4</sup>

Gamma glutamyl transpeptidase (GGTP) is found in the cell membranes of a wide distribution of tissues including liver (both hepatocytes and cholangiocytes), kidney, pancreas, spleen, heart, brain, and seminal vesicles. It is present in the serum of healthy persons. Serum levels are not different between men and women and do not rise in pregnancy. Although an elevated serum GGTP level has high sensitivity for hepatobiliary disease, its lack of specificity limits its clinical utility. The primary use of serum GGTP levels is to identify the source of an isolated elevation in the serum alkaline phosphatase level, since GGTP is not elevated in bone disease.

Any diagnostic evaluation must begin with repeating the suspect liver function tests to confirm that an abnormality does indeed exist. The history and physical are very important in narrowing the focus of the investigation and preventing a "shotgun" approach that may raise more questions than it answers. Abstinence from alcohol is required in any patient being evaluated for abnormal liver function tests, and this must be specifically addressed with the aviator. Careful attention to medications and environmental/toxic exposures may prevent the frustration of a long and expensive workup. Almost any medication can cause elevation in liver enzymes, with common offenders including NSAIDs, antibiotics, HMG CoA reductase inhibitors, and anti-tuberculous drugs. Therefore, stop current medications, whenever possible, and remove the individual from known toxic/environmental exposure sources; then assess the impact on the abnormal liver tests. This simple maneuver may answer the diagnostic questions without the need for additional testing. Most liver specialists would agree that persistent elevation of serum ALT for greater than six months is an indication to begin an investigation.

Hepatic steatosis ("fatty liver") is a common cause of aminotransferase elevation, and is unlikely to progress to cirrhosis. Weight loss is the most important aspect of treatment in obese aviators. Such fatty infiltration can often be detected by sonography, and rarely leads to aminotransferase elevations beyond four times the normal value. In steatosis, the AST/ALT ratio is at or less than 1:1. When weight loss does not result in normalization of aminotransferase levels, non-alcoholic steatohepatitis must be considered. This condition is more serious than simple hepatic steatosis, and may progress to cirrhosis. Liver biopsy is indicated for its specific diagnosis.

A 1998 report of sprue as the cause for chronically elevated aminotransferases in 13 of 140 asymptomatic patients suggests that screening for sprue with antigliadin antibodies could be valuable if more common causes of aminotransferase elevations have been excluded. Occasionally, aminotransferases can be of extra-hepatic origin, as may be the case in rhabdomyolysis. Markedly elevated CPK measurements may suggest a muscular origin of elevated aminotransferases. While severe rhabdomyolysis may cause the appearance of an acute elevation of aminotransferases, it is highly unlikely to be a cause of chronic aminotransferase elevation.

The routine measurement of serum iron/iron-binding capacity (Fe/TIBC), ceruloplasmin, and serum protein electrophoresis in patients with demonstrated aminotransferase elevations and no clear history to suggest a specific etiology may seem like a "shotgun" approach, but the conditions in question are often difficult to detect without specific

testing, and each has significant long-term implications with respect to the development of cirrhosis. A transferrin saturation of > 45% suggests hemochromatosis; the ceruloplasmin, if low, suggests Wilson's disease; and the lack of a peak alpha-globulin band on SPEP suggests alpha-1 antitrypsin deficiency. Positive antinuclear antibodies (ANA) may indicate a diagnosis of autoimmune hepatitis.

In those individuals with no firm diagnosis in spite of hepatic sonography and the battery of blood tests discussed above, focus must shift to a discussion of the need for liver biopsy and the functional status of the aviator's liver. With aminotransferases less than twice normal and well-preserved hepatic function, liver biopsy is not currently recommended.<sup>5</sup> Where aminotransferases exceed twice normal, liver biopsy may be considered to assess the extent and severity of hepatic inflammation, and of any fibrotic or cirrhotic changes. Liver biopsy should only be performed after consultation with a gastroenterologist/hepatologist. Although a liver biopsy may change the final diagnosis in some patients with nonspecific asymptomatic liver test abnormalities, modifications in management are usually minor.<sup>8</sup> In addition, liver biopsy has several well-documented drawbacks, including sampling error, variability in pathologist interpretation, cost, and morbidity. Serious complications have been noted in 0.3% of cases and mortality in 0.01%. One group in Cleveland has advocated for expectant clinical follow-up as the most cost-effective strategy in the management of asymptomatic patients with negative viral, metabolic and autoimmune markers in patients with chronically elevated aminotransferase levels. 10

Imaging techniques are being used more frequently in the early assessment of suspected liver disease. Ultrasound is typically the first-line imaging modality used in the assessment of liver function test abnormalities. CT and MRI are now being used more frequently if non-alcoholic steatohepatitis (NASH) is a suspected cause of the liver function abnormalities. A novel variation on traditional ultrasonography is the use of transient or dynamic elastography to detect hepatic fibrosis. This technique analyzes the axial propagation of a transient, mechanically generated shear wave through the liver, a process that is related to tissue elasticity or stiffness. A proprietary device called the FIBROSCAN has been studied as a non-invasive method to determine liver elasticity, and thereby to predict the presence of cirrhosis. Additional studies will be needed to validate the utility of this new technique in the assessment of patients with abnormal liver function tests.

Evaluation of abnormal aminotransferases also requires assessment of hepatic function. Demonstration of well-preserved hepatic function demands no history of encephalopathy, a physical exam free of stigmata of chronic liver disease (angiomata, palmar erythema, ascites, truncal wasting), and blood tests demonstrating preserved hepatic function. Such testing should include a normal prothrombin time, normal CBC with platelet count, and normal serum albumin. A radionuclide liver/spleen scan may add additional information when assessing liver function, since the scan can indicate overall intensity of the liver image and shunting of activity to the spleen.

While the gamma-glutamyltransferase (gamma-GT) level is so nonspecific as to provide little insight when ordered as a stand-alone test, it can be very useful when combined with other blood tests. A gamma-GT greater than two times normal in the face of an elevated AST/ALT ratio strongly suggests alcohol as the etiology of the elevated LFTs. As mentioned previously, it may also be useful in confirming the hepatic origin of an elevated alkaline phosphatase level.

A recommended test battery for patients with abnormal aminotransferases and no specific diagnosis implicated by history or physical examination consists of: AST/ALT (repeat); GGT if AST > 2X ALT; hepatitis C serologies (Hep C antibody with Hep C PCR if antibody positive); hepatitis B serologies (Hep B Surface Antigen, IgM Hep B Core Antibody); hepatitis A serology (Hep A antibody); Fe/TIBC, ferritin; ceruloplasmin; serum protein electrophoresis; hepatic sonogram (to look for ductal abnormalities or fatty infiltration); prothrombin time; CBC with platelet count; and serum albumin.

In 1901, Gilbert and Lereboullet described a syndrome of chronic, benign, intermittent jaundice, characterized by mild hyperbilirubinemia in the absence of bilirubinuria or signs or symptoms of liver disease. Gilbert's syndrome is also known as low-grade chronic hyperbilirubinemia, and is the most common of the hereditary hyperbilirubinemias (Gilbert's syndrome, Type I and Type II Crigler-Najjar syndrome, Dubin-Johnson syndrome, and Rotor's syndrome) with a genotypic prevalence of ≤12% and a phenotypic prevalence of  $\leq 7\%$ . The fact that Gilbert's syndrome is most often recognized in the second or third decades of life and rarely diagnosed before puberty appears to be attributable to pubertal changes in the plasma bilirubin concentration. <sup>12</sup> In older subjects, the diagnosis is made most often after routine screening blood tests or when fasting associated with surgery or concomitant illness unmasks the hyperbilirubinemia. Gilbert's syndrome results from defective conversion of unconjugated bilirubin to bilirubin monoand diglucuronides by a specific UDP-glucuronosyltranferase isoform designated UGT1A1 encoded on the UGT1 gene complex. Patients with Gilbert's syndrome have 10-33% of normal UGT1A1 enzymatic functioning and accounts for the typically lowlevel hyperbilirubinemia (1.5 to ~4 mg/dl). Despite earlier evidence to the contrary, Gilbert's syndrome is inherited as an autosomal recessive trait. 13

The hyperbilirubinemia in Gilbert's is mild, with plasma bilirubin levels most often less than 3mg/dl. Considerable daily fluctuation may be seen with stress, fatigue, alcohol ingestion, and concurrent illness. The plasma bilirubin may be normal on occasion in up to one-fourth of patients. Bilirubinuria is absent since the plasma bilirubin is virtually all unconjugated. Most patients with Gilbert's are asymptomatic and are unaware of the abnormality until it is detected by incidental laboratory examination or in the course of family studies. Other patients may have a variety of nonspecific symptoms, including vague abdominal discomfort, fatigue, or malaise. In general, these symptoms do not correlate with the plasma bilirubin level.

The diagnosis of Gilbert's syndrome is a diagnosis of exclusion suggested by the clinical finding of mild, chronic, unconjugated hyperbilirubinemia. Conventional hepatic biochemical tests are normal.<sup>14</sup> A family history should be sought and evidence of other

hepatic or hematological disorders, including hemolysis, excluded. Pertinent history of jaundice should include duration and previous attacks of jaundice, pain, fever, chills, or other systemic symptoms, itching, exposure to drugs (prescribed and illegal), biliary surgery, anorexia or significant weight loss, color of urine/stool, contact with other jaundiced patients, history of blood transfusions, and occupation. Caution must be exercised to eliminate the possibility that the chronic unconjugated hyperbilirubinemia is not due to some acquired disease state, such as cardiac disease, fatty liver and alcoholism, cirrhosis, biliary tract disease, viral hepatitis, malignant tumors, infections, portocaval shunts, or thyrotoxicosis. Elevated bilirubin also may be present in people living at high altitudes. Confirmed Gilbert's syndrome is usually benign in nature with an excellent prognosis. Since hyperbilirubinemia in Gilbert's may be exacerbated by fasting, it is common that a fasting chemistry profile may uncover a latent Gilbert's patient. Drawing a repeat bilirubin level on the well-hydrated (non-fasting) patient will often ease concerns caused by identification of an isolated elevation of the serum bilirubin, and avoid costly follow-up testing.

### IV. Aeromedical Concerns.

As noted above, abnormal LFTs are not of themselves disqualifying. The underlying etiology of the aminotransferase elevations must be diagnosed. Since the MSD lists "impairment of liver for any reason, if chronic and/or requiring ongoing specialty follow-up" as disqualifying, most diagnoses discussed above are disqualifying. Of the diagnoses listed, steatosis, drug-induced hepatitis, and alcohol-related liver injury are all potentially "curable". Chronic hepatitis, hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, autoimmune hepatitis, and sprue are chronic diseases with unique waiver concerns. Waiver consideration requires a firm diagnosis; once a diagnosis is made, the safety issues related to an individual so afflicted in the aerospace environment can be evaluated.

Most patients with Gilbert's syndrome are asymptomatic and should not experience problems with sudden incapacitation or mission completion. A few may experience a variety of nonspecific symptoms, including vague abdominal discomfort, nausea, diarrhea, constipation, fatigue, or malaise and will need to be individually assessed as to whether performance may be affected. If the hyperbilirubinemia is sufficiently elevated, cholelithiasis is possible.

| ICD-9 codes for abnormal liver function tests |  |  |
|---|--|--|
| 790.4   | Nonspecific elevation of levels of aminotransferase or |  |
|   | lactic acid dehydrogenase [LDH]                        |  |
| 790.6   | Other abnormal blood chemistry                         |  |
| 277.4   | Disorders of bilirubin excretion                       |  |

| ICD-10 codes for abnormal liver function tests |  |  |
|--|--|--|
| R74.0  | Nonspecific elevation of levels of aminotransferase or |  |
|  | lactic acid dehydrogenase [LDH]                        |  |
| R79.89   | Other specified abnormal findings of blood chemistry   |  |
| E80.7  | Disorder of bilirubin metabolism, unspecified          |  |

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### WAIVER GUIDE

Updated: Mar 2015

Supersedes Waiver Guide of Jan 2011

By: Capt Vanessa Pearson (RAM 16) and Dr Dan Van Syoc

Reviewed by: Lt Col Nicholas Conger, AF/SG consultant in Infectious Diseases

## **CONDITION:**

Lyme Disease (Mar 2015)

## I. Waiver Considerations.

Patients should be DNIF while symptomatic and under treatment. Once all symptoms of the disease have resolved, the aviator can be returned to status without a waiver (true for all aviation classes). Lyme disease is not mentioned by name as disqualifying for any aviation class, but the residual symptoms mentioned in Section III may require a waiver. In these cases, waiver for flying classes I/IA, II, and III, as well as for ATC, GBO and SWA personnel may be considered, depending on the success of the therapy. An ACS review of cardiologic or neurologic complications is recommended.

Table 1: Waiver potential for Lyme disease

| Flying Class  | Condition         | Waiver Potential | ACS               |
|---------------|-------------------|------------------|-------------------|
|               |                   | Waiver Authority | review/evaluation |
| I/IA          | Stage II and III  | Yes*             | Yes               |
|               | Lyme disease with | AETC             |                   |
|               | complications or  |                  |                   |
|               | residual symptoms |                  |                   |
| II/III        | Stage II and III  | Yes*             | Yes               |
|               | Lyme disease with | MAJCOM           |                   |
|               | complications or  |                  |                   |
|               | residual symptoms |                  |                   |
| ATC, GBO, and | Stage II and III  | Yes*             | Yes               |
| SWA           | Lyme disease with | MAJCOM           |                   |
|               | complications or  |                  |                   |
|               | residual symptoms |                  |                   |

<sup>\*</sup>FC I/IA candidates and all other initial training candidates need to be totally disease and complication free for at least 12 months prior to waiver consideration. Waiver authority in such cases is AETC.

Review of the AIMWTS data base through Nov 14 revealed a total of 8 cases submitted for waiver consideration with the diagnosis of Lyme disease. There was 1 FC I case, 4 FC II cases, 2 FC III cases, and 1 MOD case. All were granted waivers except for the MOD case which resulted in a disqualification for persistent neurological symptoms.

## II. Information Required for Waiver Submission.

The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for cardiology involvement should include:

- A. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- B. Copies of reports and tracings/images of any cardiac tests (e.g. electrocardiogram, echocardiogram, treadmill, Holter monitor, cardiac cath, cardiac CT or MRI) performed locally for clinical assessment (i.e., serial ECGs for uncomplicated 2<sup>nd</sup> degree AV blocks; serial Holters/echos depending on the level of cardiac involvement to begin with; etc.). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- C. Any procedure-related reports (e.g. pacers, EP studies, etc.), as applicable.
- D. Results of serologic studies.

Note 1: Call ACS to get correct mailing address for all required videotapes and CDs. For expediting the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

The aeromedical summary for neurological involvement should include:

- A. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- B. Neurology consultation report.
- C. Neuropsych testing, as appropriate.
- D. Results of serologic studies.

The aeromedical summary for arthritic involvement should include:

- A. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level.
- B. Rheumatology consultation report.
- C. Results of serologic studies.

#### III. Overview.

Lyme disease is the most common tick-borne disease in the United States (U.S.).<sup>1,2</sup> In North America, it is caused exclusively by the spirochete *Borrelia burgdorferi* whereas in Europe it is caused by *B. afzelii*, *B. garinii*, *B. burgdorferi*, and occasionally by other species of borrelia.<sup>2</sup> It occurs worldwide and has been reported on every continent except Antartica.<sup>1</sup> Lyme disease surveillance in the U.S. began in 1982 at the Centers for Disease Control (CDC) and became a nationally reportable disease in 1991. In the U.S., the number of reported cases has been steadily increasing from over 11,700 cases/year in 1995 to almost 30,000 cases/year in 2009. Since 2009, the number of cases decreased to less than 25,000 in 2010, 2011, and 2012, but there was an increase again in 2013 to more than 27,000 (these numbers only reflect the number of confirmed cases not the number of probable cases).<sup>3</sup> In 2013, the highest number of confirmed Lyme cases were in Pennsylvania (4,981), Massachusetts (3,816), New York (3,512), New Jersey (2,785), and Connecticut (2,111).<sup>4</sup> In the Northeastern and North-central U.S., the black-legged tick (or deer tick, *Ixodes scapularis*) transmits Lyme disease and in the Pacific coastal U.S.,

the disease is spread by the western black-legged tick (*Ixodes pacificus*). A cluster of cases identified in 1975 had their epidemiological epicenter in Lyme, Connecticut, for which the disease was named.<sup>5</sup> Documentation of this disease dates back to 1883 in Breslau, Germany by a physician named Alfred Buchwald. He described an expanding, ring like lesion now known as erythema migrans (EM), the most common symptom associated with early Lyme disease, and speculated that the rash came from the bite of an *Ixodes* tick.<sup>6</sup>

Three distinct foci occur in the United States: the Northeast (Maine to Maryland), the North Central (Wisconsin and Minnesota) and the West (northern California and Oregon). In Europe, most cases occur in the Scandinavian countries and in central Europe (Germany, Austria, and Switzerland), although cases have been reported in the United Kingdom (South Downs and New Forest areas). Other prevalent worldwide locations include Russia, China and Japan.

The ticks have larval, nymphal and adult stages, each stage requiring a blood meal. In the Northeast and North Central U.S., an efficient cycle of infection of *B. burgdorferi* between nymphal ticks and white footed mice yields a high frequency of infection during the spring and summer months in humans. An abundance of deer, the adult ticks' preferred host, fulfill a similar role in the Northeast. *I. scapularis*, also known as *I. dammini*, serves as the tick vector. The principle vector in the Northwestern U.S. is *I. pacificus*. The frequency of human infection is relatively low in the Northwest, as *I. pacificus* tends to feed on lizards, which are not susceptible to the infection, and only occasionally feed on the dusky-footed woodrat while in the larval stage. In Europe and Asia the principal vectors include *I. ricinus* and *I. persulcatus*, respectively, which also serve as vectors of tick-borne encephalitis virus.

Even though the likelihood of infection is twice as high in adult ticks than in the nymphal stage, most cases of transmission of early Lyme disease occur in the spring and summer months when the nymph is seeking a blood meal. Adult ticks are much larger and easier to identify and remove prior to transmission of infection. Animal studies confirm that approximately 36 - 72 hours are required for transmission of the infection to the animal host once the tick has attached itself to the host. During this time spirochetes in the midgut of the tick multiply and migrate to the tick's salivary glands, in preparation for transmission to the animal host. Only ticks that are partially engorged with blood are associated with the development of EM at the site of the bite.

Active Lyme disease occurs in three broad stages. The clinical symptoms of each stage may overlap. Individuals may also present in a later stage without presenting with symptoms of an earlier stage. <sup>9, 11</sup> In addition, there is a post-Lyme disease syndrome the practitioner should be aware of the includes nonspecific symptoms such as headache, fatigue, and joint pain that may linger for months. <sup>11</sup> The most common clinical manifestation of the first phase is EM. <sup>2</sup> EM occurs between 3 and 30 days, although it most commonly develops between 7 and 14 days. In the U.S., EM (single or multiple) is found in about 90% of patients with objective evidence of infection with *B. burgdorferi*. <sup>12</sup> This lesion is usually greater than or equal to 5 cm in diameter, often with a central

clearing, bull's-eye or target like appearance. Approximately 45 percent of patients with EM have spirochetemia which is not related to the size or duration of the presenting skin lesion.<sup>5</sup> Hematogenous dissemination from the primary infection site may yield secondary lesions.

Lyme disease has a myriad of dermatologic, neurologic, cardiac, and musculoskeletal manifestations. The most common symptoms during the primary stage often resemble those of a viral infection, including myalgias, arthralgias, fatigue, headache, neck pain and possible fever. Rarely, respiratory, gastrointestinal or ocular complaints such as conjunctivitis, iritis, and keratitis may be reported.<sup>2, 5, 13</sup> EM spontaneously resolves in approximately four weeks without treatment.<sup>8</sup> Given these vague initial symptoms, this represents a challenge in early detection and initial treatment.

The second stage is manifested by dissemination of the disease within days up to 10 months following the initial tick bite. 9, 11 It is associated with hematogenous spread of the spirochete to extracutaneous sites. Treatment at this stage helps to prevent later problems associated with Lyme disease. 11 Sixty percent of untreated patients with EM will progress to mono or oligoarticular arthritis, usually involving the knee. Ten percent will manifest with neurologic complications, the most common of which is facial-nerve palsy. Neurologic involvement may occur within weeks. Acute neuroborreliosis may develop in up to 15 percent of untreated patients in the U.S. Potential manifestations include lymphocytic meningitis with episodic headache and mild neck stiffness, subtle encephalitis with difficulty with mentation, cranial neuropathy (particularly unilateral or bilateral facial palsy), motor or sensory radiculoneuritis, mononeuritis multiplex, cerebellar ataxia or myelitis. In children blindness may result secondary to increased intracranial pressure on the optic nerve. Acute neurologic abnormalities spontaneously improve or resolve over a period of weeks or months, even in untreated patients. Cardiac involvement may occur several weeks after the initial onset. Approximately five percent of untreated patients experience cardiac involvement, to include atrioventricular block, acute myopericarditis, mild left ventricular dysfunction and rarely cardiomegaly or fatal pancarditis.<sup>9, 11</sup>

The third stage includes late disease which may occur months to years following the initial tick bite. <sup>9, 11</sup> In some individuals, symptoms at this stage may be the first symptoms of the disease. <sup>11</sup> Individuals experiencing joint involvement may sustain several brief attacks of arthritis with the potential for persistent joint inflammation. In up to 10 percent of cases, the arthritis may persist for months or years despite 30 days of intravenous (IV) or 60 days of treatment with oral antibiotics. <sup>5</sup> Large joints, especially the knee are susceptible, presenting with joint swelling and pain which is thought to be mediated by the immune response by the spirochete in the joint. <sup>13</sup> Up to five percent of untreated patients may experience chronic neuroborreliosis. This may occur after long periods of latent infection. In the U.S. and Europe, a chronic axonal polyneuropathy may develop manifesting as spinal radicular pain or distal paresthesia. In Europe, chronic encephalomyelitis may occur. It is most often characterized by spastic paraparesis, cranial neuropathy or cognitive impairment with marked intrathecal production of antibodies against the

spirochete. In the U.S., Lyme encephalopathy, a mild, late neurologic syndrome with subtle cognitive disturbances, has been reported.<sup>8</sup>

Diagnosis in the U.S. is usually based on the recognition of the characteristic clinical findings, a history of exposure in an area where the disease is endemic and except in patients with erythema migrans, an antibody response to *B. burgdorferi* by enzyme-linked immunosorbent assay (ELISA) and Western blotting. IgM antibody titers during the first month of infection are unreliable. IgG antibody responses are prevalent in most patients infected for one month. Even with antibiotic treatment, IgM and IgG titers may persist for many years.<sup>8</sup>

Treatment recommendations during the first stage of Lyme disease include: doxycycline 100 mg twice daily for adults; amoxicillin 500 mg three times daily for adults; or cefuroxime axetil 500 mg twice daily for adults. The duration of therapy has traditionally been three weeks, although some studies suggest that a 10 to 14 day duration of therapy may be as effective. Doxycycline is not recommended for children under 8 years of age or for pregnant or lactating women. Individuals with chronic musculoskeletal pain, neurocognitive symptoms or both that persist after antibiotic treatment for well-documented Lyme disease may have considerable impairment in their health-related quality of life. However further treatment with an extended (90 day) course of antibiotics in a controlled clinical trial in individuals without evidence of persistent infection by *B. burgdorferi* received no added benefit over those who received placebo. A substantial increase in the risk of morbidity and even death in patients secondary to extended antimicrobial therapy was noted in this study. <sup>15</sup>

Second (early disseminated) and third (late) stages of Lyme disease may be treated with intravenous (IV) ceftriaxone, a third generation cephalosporin. Recommended dosages include 2 g once daily in adults. Similarly, cefotaxime 2 g every eight hours is also recommended in adults. Additionally, penicillin G divided into doses given every four hours in patients with normal renal function may be effectively used. Eighteen to 24 million units per day in adults is the recommended dosage. Recommended duration of IV therapy is two to four weeks. Four weeks is the current standard in many communities, although there is no evidence to support greater efficacy of four versus two weeks. There is also no evidence that treating for more than four weeks is beneficial. However, a 28-day course is preferred if the patient suffers from facial nerve palsy that has not resolved within 14 days. <sup>14</sup>

Prevention may be accomplished through avoidance of tick-infested areas, wear of protective clothing, the use of repellents and acaricides, tick checks and modifications of landscapes in or near residential areas. In December 1998, GlaxoSmith-Kline gained U.S. Food and Drug Administration approval for a *B. burgdorferi* outer surface protein A (OspA)-based Lyme disease vaccine, LYMErix. The efficacy was 49 percent after two injections and 76 percent after three injections. The vaccine, however, was voluntarily withdrawn from the market because of poor sales. Antimicrobial treatment within 72 hours of a tick bite with a single 200 mg dose of doxycycline has been suggested as effective prophylaxis against the development of Lyme disease. Although a study

reported an efficacy of 87 percent, it was limited by the number of participants in whom Lyme disease developed, resulting in a wide 95 percent confidence interval. This study is in direct contrast to other studies demonstrating no clear protection attributable to antimicrobial prophylaxis administered after a tick bite. Regardless, it may be prudent in aircrew to consider doxycycline prophylaxis within 72 hours of a tick bite from an endemic area to preclude progression of possible Lyme disease, since doxycycline is an approved aircrew medication after ground testing.

#### IV. Aeromedical Concerns.

The symptoms during primary Lyme disease, including arthralgias, fatigue, headache, neck pain and possible fever are obviously not optimal in the flying environment. As with all infectious diseases, if recognized and treated early with full resolution of symptoms, return to flight status is appropriate. However, if untreated, then aeromedical concerns of this disease are its debilitating effects in regards to the neurologic, cardiovascular, and arthritides that may result. Neurocognitive impairment, cardiac arrhythmias and arthritic pain are all manifestations that could impact the safety of the individual and mission.

| ICD-9 code for Lyme disease |              |
|-----------------------------|--------------|
| 088.81                      | Lyme disease |

| ICD-10 code for Lyme disease     |  |
|----------------------------------|--|
| A69.20 Lyme disease, unspecified |  |

#### V. References.

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## Malaria/Antimalarials (Feb 2019)

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**Significant Changes:** Atovaquone/proguanil is acceptable USAF 1<sup>st</sup> line agent

## I. Waiver & Operational Considerations

Malaria infection is not waiverable and any aircrew or special duty operator who contracts malaria requires DNIF or DNIC until successfully treated and fully recovered. There are several medications for malaria prophylaxis that are approved for aeromedical and operational use without a waiver. These medications can be found in the "Official Air Force Aerospace Medicine Approved Medications List." The approved medications currently are chloroquine (Aralen®), doxycycline (Vibramycin®), primaquine (PQ), and atovaquone/proguanil (Malarone®). Ground testing is required to exclude idiosyncratic reactions, and the parameters differ between medications. MEFLOQUINE (Larium®) IS NOT APPROVED. If mefloquine is mistakenly administered, a DNIF/DNIC period of four weeks is required to observe for the development of neuropsychological side effects.

There are a variety of factors that will influence decision-making regarding malarial prophylaxis. Choice of an appropriate antimalarial depends on the distribution of *Plasmodium* spp. in the area(s) that will be traveled through, local drug resistance patterns, and length of anticipated exposure. Timing will also influence antimalarial choice. Some of the approved prophylaxis agents require initiation up to a week before travel, and the length of terminal prophylaxis after return from the endemic area also varies. For travel or deployment with short notice, one of the medications that does not require preloading would be preferred. Other factors that will influence aeromedical decision-making include the availability of established medical infrastructure at the destination and individual tolerability, side effects, or contraindications of the particular medications. Currently, there is no unified policy regarding malaria prophylaxis in USAF personnel. Different MAJCOMs or theater commanders may implement specific policies with consideration for the unique nature of their mission.

#### II. Information Required for Waiver Submittal

Not Applicable.

#### III. Aeromedical Concerns

The prescribing of antimalarial medications by flight medicine providers for use in USAF aircrew and special duty operators is common due to the frequency of deployments to malaria endemic areas. To prevent malaria and to maintain the health and operational readiness of aircrew and special duty operators, a proper understanding of this disease and

the use of antimalarial chemoprophylaxis is essential. Malaria comprises at least five protozoan species transmitted by female anophelene mosquitoes that bite primarily in the dark hours from dusk to dawn. *Plasmodium falciparum* may be rapidly fatal in nonimmune visitors to endemic areas; the other species (most commonly *P. vivax*, *P. ovale*) much less commonly cause severe disease, but infected individuals may relapse many weeks to months after exposure due to latent infection harbored in the liver. Both primary and relapsing malaria represent infection of erythrocytes—with multiple attendant complications—resulting at least in an uncomfortable, febrile syndrome that is incompatible with the aviation or operational environment.

Prevention is the first and best line of defense against malaria, including personal protective measures combined with strategies to avoid mosquito bites. Appropriate antimalarial chemoprohylaxis taken correctly should prevent clinical malaria disease during travel, but malaria infection can occur if the above protective measures fail and/or doses of chemoprophylaxis are missed. Malaria that is acquired while taking chemoprophylaxis may be atypical in presentation, delayed in onset, and more difficult to diagnose and differentiate from other illnesses. Relapsing forms of malaria (non-falciparum species) are prevented and cleared of their latent hepatic forms only by primaquine, its use variably termed "terminal prophylaxis," "presumptive antirelapse therapy," or "radical cure."

Among the available chemoprophylactic agents, mefloquine (Larium®) is NOT APPROVED FOR USE due to potential neuropsychiatric side effects. Given its long half-life, members taking mefloquine by mistake must remain DNIF/DNIC for four weeks and observed for adverse effects. Mefloquine is contraindicated for anyone with significant psychiatric history or cardiac conduction abnormality. Chemoprophylaxis approved for use by aircrew or special duty operators includes chloroquine (Aralen®), doxycycline (Vibramycin®), atovaquone/proguanil (Malarone®), and primaquine (PQ).

Chloroquine has a long half-life, making it appropriate for weekly dosing. Ground trial is required due to potential side effects such as nausea, abdominal discomfort, palpitations, agranulocytosis (or multiple cytopenias), headache, lightheadedness, ataxia, vertigo, tinnitus, sensorineural hearing loss, diarrhea, pruritus, fatigue, and visual symptoms (accommodation disturbance, blurred vision, scotoma, color vision changes, and visual field defects). Chloroquine may suppress the cell-mediated immune response, contributing to complications such as reactivation herpes viruses (e.g. zoster). Personnel experiencing significant neurological side effects must remain DNIF/DNIC for four weeks while observed for side effect resolution. Members taking chloroquine for longer than several months should be examined periodically for visual adverse effects, including acuity and color discrimination. Although FDA indicated for malaria chemoprophylaxis, hydroxychloroquine currently is not approved for use in aircrew or special duty operators for the purpose of malaria prevention. Its use for this indication requires a waiver. Hydroxychloroquine has an adverse effect profile that is similar to chloroquine; both may prolong the QTc interval. In areas with chloroquine-sensitive P. falciparum, both chloroquine and hydroxychloroquine in adults is administered once weekly beginning one to two weeks prior to exposure, during exposure, and for four weeks following exposure.

<u>Doxycycline</u> is a daily chemoprophylaxis agent with a half-life so short that it needs to be taken reliably every 24 hours (regardless of number of time zones crossed). Ground trial is required to detect idiosyncratic reactions and demonstrate tolerability. Common adverse effects include gastrointestinal upset (ameliorated by taking with food), headache, tinnitus, photosensitivity, and vulvovaginal candidiasis. Pill esophagitis is a rare complication which can be avoided by taking with plenty of fluids and avoiding recumbence immediately after a dose. Doxycycline in adults is administered once daily beginning one to two days prior to exposure, during exposure, and for four weeks following exposure.

Atovaquone/proguanil (AP) is a daily chemoprophylaxis agent that has a low rate of discontinuation due to side effects. Single-dose ground trial is required. Adverse effects may include nausea, abdominal discomfort, and headache; but photosensitivity and neuropsychiatric manifestations are not characteristic. AP represents a more expensive malaria prophylaxis option, but it may be required preferentially for some regions (e.g., USAFRICOM AOR). AP in adults is administered once daily beginning one to two days prior to exposure, during exposure, and for one week following exposure.

Primaquine (PQ) generally is reserved for terminal prophylaxis after travel to areas in which there is significant risk for exposure to non-falciparum malaria (relapsing species). PQ use per policy (e.g., for Force Health Protection purposes) must be in accordance with FDA indications, i.e. 15 mg base daily for two weeks. However, the clinical (non-policy) off-label dosing of 30 mg daily for two weeks is more commonly used and widely accepted among travel medicine practitioners. PQ has also been used (similarly off-label) as a 30 mg daily primary chemoprophylaxis agent in areas without reported *P. falciparum*. Specifically, for short duration travel to areas with principally *P. vivax*, PQ is administered once daily beginning one to two days prior to exposure, during exposure, and for one week following exposure. G6PD activity must be assessed prior to any PQ use, and PQ is not recommended for pregnant or breastfeeding women due to the unknown G6PD status of the infant. Single-dose ground trial is required prior to aircrew or operational use. Adverse effects may include abdominal discomfort, nausea, rash, headache, pruritus, interference with accommodation, cytopenias (even in G6PD-normal individuals), and methemoglobinemia.

#### IV. Suggested Readings

Resources available to the flight medicine provider caring for individuals who may be traveling to or deploying to at-risk locations include those listed below.

Centers for Disease Control and Prevention

<u>https://www.cdc.gov/malaria/about/distribution.html</u> (geographic distribution)
<u>https://www.cdc.gov/malaria/travelers/country\_table/a.html</u> (drug resistance by country)

Yellow Book: Health Information for International Travel (CDC publication) <a href="https://wwwnc.cdc.gov/travel">https://wwwnc.cdc.gov/travel</a>

Travax, US DoD website for operational travel medicine (CAC required)

# https://private.travax.com

National Center for Medical Intelligence, Defense Intelligence Agency (CAC required)

<a href="https://www.ncmi.detrick.army.mil/">https://www.ncmi.detrick.army.mil/</a> (Force Health Protection information)

Armed Forces Pest Management Board

https://www.acq.osd.mil/eie/afpmb/

Malaria Field Guide (US Army Public Health Command publication)

https://www.africom.mil/doc/25326/malaria-field-guide

World Health Organization. Guidelines for the treatment of malaria, 3rd ed. WHO, Geneva, 2015.

http://www.who.int/malaria/publications/atoz/9789241549127/en/

## WAIVER GUIDE

Updated: Apr 2016

Supersedes Waiver Guide of Jul 2015

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Medicine), and Dr Dan Van Syoc

Reviewed by: Lt Col Jeffrey Bidinger, AF/SG consultant for Dermatology

## **CONDITION:**

Malignant Melanoma (Apr 2016)

## I. Waiver Considerations

History of melanoma is disqualifying for all flying classes; as all malignancies require an MEB. The table below outlines the waiver potential for flying class (FC) I/IA, II, and III based on AJCC melanoma staging system.

Table 1: Waiver potential based on flying class and melanoma stage.

| Flying Class   | Melanoma Stage               | <b>Waiver Potential</b> | ACS                |
|----------------|------------------------------|-------------------------|--------------------|
|                | <b>Including History of</b>  | Waiver                  | Review/Evaluation  |
|                | ·                            | Authority‡              |                    |
| I/IA           | 0                            | Maybe#†                 | No                 |
|                |                              | AETC                    |                    |
|                | IA, IB, IIA, IIB, IIC, IIIA, | No                      | No                 |
|                | IIIB, IIIC, IV               | AETC                    | 110                |
| II (pilot)     | 0, IA, IB                    | Yes†                    | Yes (Stage IA, IB) |
|                |                              | MAJCOM‡                 |                    |
|                | IIA, IIB, IIIA               | Maybe*                  | Yes                |
|                |                              | MAJCOM‡                 |                    |
|                | IIC, IIIB, IIIC, IV          | No                      | No                 |
|                |                              | MAJCOM‡                 |                    |
| II (non-pilot) | 0, IA, IB                    | Yes†\$                  | Yes (Stage IA, IB) |
| III            |                              | MAJCOM‡                 |                    |
| ATC            |                              |                         |                    |
| GBO            | IIA, IIB, IIIA, IIC, IIIB,   | Maybe*                  | Yes                |
| SWA            | IIIC                         | MAJCOM‡                 |                    |
|                |                              | No                      | No                 |
|                | IV                           | MAJCOM‡                 |                    |

<sup>#</sup> Waiver may be considered if no risk factors such as history of dysplastic nevus syndrome (greater than 50 atypical nevi, family history of atypical nevi and family history of melanoma) are present.

All waivered cases require close follow-up for life, at intervals recommended by the evaluating dermatologist or oncologist, at least annually.

AIMWTS review through Feb 2016 revealed 324 cases of melanoma. Breakdown of these cases revealed: 6 FC I/IA cases (3 disqualified), 209 FC II cases (14 disqualified), 80 FC III cases (11 disqualified), 8 ATC/GBC cases (no disqualifications), and 20 MOD cases (1 disqualified). Of these, 286 (91%) received waivers and 29 (9%) were disqualified; the vast majority approved were Stage 0 or IA.

<sup>†</sup> Waiver may be considered by waiver authority 6-months post-completion of definitive treatments. No indefinite waivers will be granted except for Stage 0.

<sup>\$</sup> Waiver in untrained FC II/III/ATC/GBO/SWA personnel with stage 0, stage IA, or stage IB melanoma may be considered after member has been disease free for three years if no risk factors such as history of dysplastic nevus syndrome (greater than 50 atypical nevi, family history of atypical nevi and family history of melanoma) are present.

<sup>\*</sup> Waiver may be considered by waiver authority three years post-completion of definitive treatments, if clinically stable with no evidence of local or distant recurrence.

<sup>‡</sup> For all except FC I/IA, AFMRA is the initial waiver authority for malignant neoplasms.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for initial waiver should include the following:

- A. History summary of disease course, risk factors, review of systems, and activity level.
- B. Physical special attention to skin and lymph nodes. Need to also exam fundus and conjunctiva.
- C. Dermatological consultation (and oncology/surgery consultation if indicated), with specific comments regarding work-up to rule-out metastatic disease.
- D. Pathology report, specifically indicating histologic diagnosis of melanoma, presence or absence of tumor ulceration, and tumor thickness (AJCC melanoma staging system).
- E. Confirmation of histology, ulceration, and thickness by AFIP or a DoD accredited dermatopathologist, with a copy of report attached.
- F. Copies of all laboratory studies, radiological studies, and any other studies.
- G. Statement that incision site does not interfere with flying duties and wearing of aircrew flying and life-support equipment.
- H. Medical evaluation board (MEB) report.
- I. Outline plan for follow-up.

The AMS for waiver renewal should include the following:

- A. History AJCC melanoma staging, interval frequency and results, and review of systems.
- B. Physical skin and lymph node. Need to also exam fundus and conjunctiva.
- C. Dermatology consult to include follow-up plan.

## III. Overview.

Melanoma accounts for just 7% of all dermatological cancers and it is curable in early stages, but it causes 73-80% of all deaths from skin cancer. According to recent data, melanoma is the fifth and sixth most common new cancer diagnosis among men and women in the United States, respectively. In 2014, there were 76,100 new cases of melanoma diagnosed and 9,710 deaths (1.7% of all cancer-related deaths) in the United States. It is also the second leading cause of lost productive years among cancers. The incidence of melanoma continues to climb, with estimated increases of 2-4%, annually. Risk factors for melanoma include family history of melanoma, fair skin, light eyes, red or blonde hair, a predisposition to sunburns, history of extensive sunlight exposure, a history of at least one episode of a severe sunburn before the age of 18 (two- to three-fold increase in risk), a greater number of common nevi, dense freckling, immunosuppression, and advancing age. Melanoma is of particular concern in the aviator population because it is one of the few malignancies that is often diagnosed in young and middle-aged persons. In fact, the incidence of cutaneous melanoma among middle-aged adults increased over the last forty years.

Melanoma is the 3<sup>rd</sup> leading cause of brain metastasis after lung and breast cancer. Older studies suggested an approximately 13-20% risk of brain metastasis as first site of recurrence among those who eventually relapse.<sup>6,7</sup> However, a more recent, prospective study of 900 melanoma patients found only a 10% incidence of brain metastasis over the period of the study (Aug 2002-Oct 2008).<sup>8</sup> Similarly, another retrospective review of the medical records of 211 patients who experienced a first recurrence of melanoma after definitive treatment of the initial malignancy demonstrated that 8% presented with the brain as the initial site of involvement.<sup>9</sup> In a study of 81 individuals with brain metastasis, 48% experienced seizures while 21% had seizures as the first manifestation of the brain metastasis.<sup>10</sup> In another study of 702 individuals with clinically significant brain metastasis, initial presentation included 39% with focal neurological symptoms, 13% with seizures, 3% with neurological catastrophes, and 2% with behavioral changes, all of which are of major concern in flight.<sup>11</sup>

Screening for melanoma in high-risk individuals in the primary care setting is considered cost effective and results in earlier diagnosis, which correlates with improved survival. <sup>12</sup> Clinical features used to screen for melanoma include mole **a**symmetry, **b**order irregularity or poor definition, **c**olor variation, **d**iameter larger than 6 mm, and **e**volving features (the ABCDEs). Suspicion is raised when a lesion appears different from other moles or undergoes changes, such as increasing size, asymmetric growth, an irregular pigment pattern or network, development of white, gray, or black areas, bleeding, itching or tenderness within the pigmented lesion. <sup>3</sup>

Excisional biopsy of the entire suspicious lesion should be performed and tissue submitted to pathology. It is of paramount importance to excise the lesion in its entirety and avoid bisecting any suspicious nevus so that an adequate depth can be assessed on pathologic analysis.<sup>3</sup> After melanoma is histologically confirmed, pathologic staging determines prognosis and treatment. The most powerful negative predictors of survival are greater thickness of the lesion, presence of ulceration, and high mitotic index. 13, 14, 15, 16 Other important factors include microsatellite instability, in-transit metastasis, lymph node involvement, and distant metastasis. 16, 17 Additional factors that are generally associated with a worse prognosis but are of less certain significance include anatomic site (trunk location worse than extremities), male gender, histologic subtype, presence of lymphovascular invasion or perineural invasion, and regression of the primary tumor. The presence of tumor-infiltrating lymphocytes shows potentially better survival outcomes. <sup>16</sup> If multiple primary melanomas are present, staging is classified according to the primary lesion demonstrating the worst prognostic features. 18 The characteristics of the primary lesion that are more likely to be associated with CNS metastasis are location of the primary lesion in the mucosal, head, neck or trunk area, acral lentiginous or nodular histologic subtypes, presence of lymph node involvement, or metastatic spread to the viscera.<sup>11</sup>

The 2009 American Joint Committee on Cancer Staging System (AJCC) for Melanoma reflects that the histological features of primary melanoma (thickness, mitotic rate, and ulceration) are important hallmarks for prognosis and staging.<sup>13, 19</sup>

| Classification | Thickness (mm)  | Ulceration Status/Mitoses  |
|----------------|---|--|
| T              |   |  |
| Tis            | NA  | NA   |
| T1             | ≤ 1.00  | a: Without ulceration and mitosis < 1/mm² b: With ulceration or mitoses ≥ 1/mm²      |
| T2             | 1.01-2.00   | a: Without ulceration<br>b: With ulceration  |
| Т3             | 2.01-4.00   | a: Without ulceration<br>b: With ulceration  |
| T4             | > 4.00  | a: Without ulceration<br>b: With ulceration  |
| N              | No. of Metastatic Nodes   | Nodal Metastatic Burden  |
| N0             | 0   | NA   |
| N1             | 1   | a: Micrometastasis*  |
|                |   | b: Macrometastasis†  |
| N2             | 2-3   | a: Micrometastasis*  |
|                |   | b: Macrometastasis†  |
|                |   | <ul> <li>c: In transit metastases/satellites<br/>without metastatic nodes</li> </ul> |
| N3             | 4+ metastatic nodes, or<br>matted nodes, or in<br>transit<br>metastases/satellites<br>with metastatic nodes |  |
| М              | Site  | Serum LDH  |
| M0             | No distant metastases   | NA   |
| M1a            | Distant skin, subcutaneous, or nodal metastases   | Normal   |
| M1b            | Lung metastases   | Normal   |
| M1c            | All other visceral metastases   | Normal   |
|                | Any distant metastasis  | Elevated   |

Abbreviations: NA, not applicable; LDH, lactate dehydrogenase. "Micrometastases are diagnosed after sentinel lymph node biopsy. †Macrometastases are defined as clinically detectable nodal metastases confirmed pathologically.

Table 2. Anatomic Stage Groupings for Cutaneous Melanoma

| Clinical Staging* |                                       | ging  |   | Pathologic StagingT   |  |   |
|-------------------|---------------------------------------|---|---|---|--|---|
| Т                 | Ν                                     | M   |   | Т   | Ν  | Μ   |
| Tis               | N0                                    | M0  | 0   | Tis   | N0   | M0  |
| T1a               | N0                                    | M0  | IA  | T1a   | N0   | M0  |
| T1b               | N0                                    | M0  | IB  | T1b   | N0   | M0  |
| T2a               | N0                                    | M0  |   | T2a   | N0   | M0  |
| T2b               | N0                                    | M0  | IIA   | T2b   | N0   | M0  |
| ТЗа               | N0                                    | M0  |   | T3a   | N0   | M0  |
| T3b               | N0                                    | M0  | IIB   | T3b   | N0   | M0  |
| T4a               | N0                                    | M0  |   | T4a   | N0   | M0  |
| T4b               | N0                                    | M0  | IIC   | T4b   | N0   | M0  |
| Any T             | N > N0                                | M0  | IIIA  | T1-4a   | N1a  | M0  |
|                   |                                       |   |   | T1-4a   | N2a  | M0  |
|                   |                                       |   | IIIB  | T1-4b   | N1a  | M0  |
|                   |                                       |   |   | T1-4b   | N2a  | M0  |
|                   |                                       |   |   | T1-4a   | N1b  | M0  |
|                   |                                       |   |   | T1-4a   | N2b  | M0  |
|                   |                                       |   |   | T1-4a   | N2c  | M0  |
|                   |                                       |   | IIIC  | T1-4b   | N1b  | M0  |
|                   |                                       |   |   | T1-4b   | N2b  | M0  |
|                   | T Tis T1a T1b T2a T2b T3a T3b T4a T4b | T N  Tis N0  T1a N0  T1b N0  T2a N0  T2b N0  T3a N0  T3b N0  T4a N0  T4b N0 | T N M Tis N0 M0 T1a N0 M0 T1b N0 M0 T2a N0 M0 T2b N0 M0 T3a N0 M0 T3b N0 M0 T4a N0 M0 T4b N0 M0 T4b N0 M0 | T N M  Tis N0 M0 0 T1a N0 M0 IA T1b N0 M0 IB T2a N0 M0 IIA T2b N0 M0 IIA T3a N0 M0 T3b N0 M0 IIB T4a N0 M0 T4b N0 M0 IIC Any T N > N0 M0 IIIA | T N M T  Tis N0 M0 0 Tis  T1a N0 M0 IA T1a  T1b N0 M0 IB T1b  T2a N0 M0 IZa  T2b N0 M0 IZa  T2b N0 M0 IZa  T2b N0 M0 IZa  T3a N0 M0 T3a  T3b N0 M0 IZA  T4a N0 M0 IZA  T4b IZB  T1-4a  T1-4a | T N M T N  Tis N0 M0 0 Tis N0  T1a N0 M0 IA T1a N0  T1b N0 M0 IB T1b N0  T2a N0 M0 IB T1b N0  T2b N0 M0 IB T2b N0  T3a N0 M0 T3a N0  T3b N0 M0 IIB T3b N0  T4a N0 M0 T4a N0  T4b N0 M0 IIC T4b N0  Any T N > N0 M0 IIIA T1-4a N1a  T1-4b N2a  IIIB T1-4b N1a  T1-4a N2b  T1-4a N2b  T1-4a N2c  IIIC T1-4b N1b |

<sup>\*</sup>Clinical staging includes microstaging of the primary melanoma and clinical/ radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

M1 IV

Any T Any N

IV

T1-4b N2c

Any T N3

 $\mathsf{Any}\,\mathsf{T}\quad\mathsf{Any}\,\mathsf{N}$ 

M0

M0

M1

regional and distant metastases.

†Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial (ie, sentinel node biopsy) or complete lymphadenectomy. Pathologic stage 0 or stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.

The primary treatment for all melanomas is wide local excision. Sentinel lymph node biopsy is recommended in any melanoma with high risk features for improved prognostic staging and to guide additional therapy.<sup>3</sup> Systemic adjuvant therapy remains a treatment option for metastatic disease. This includes cytotoxic chemotherapy, immunotherapy, or the combination of both. However, some of these drugs convey significant risk of toxicity with unclear survival benefit.<sup>20</sup>

#### IV. Aeromedical Concerns.

Aeromedical concerns in the case of treated malignant melanoma center on both the risk of an in-flight incapacitating event and the risk of subtle performance decrement resulting from a recurrence of disease affecting the CNS. Other factors that must be considered prior to granting a waiver include the impact of surgical wounds, scars, or skin grafts on range of motion and proper/comfortable fit of flying/life support equipment.

| ICD-9 code for Malignant Melanoma |  |  |
|-----------------------------------|--|--|
| Malignant melanoma of the skin    |  |  |

| ICD-10 codes for Malignant Melanoma |   |  |
|-------------------------------------|---|--|
| C43.9                               | Malignant melanoma of the skin, unspecified |  |
| D03.9                               | Melanoma in situ                            |  |

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## Meningitis and Encephalitis (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

#### **Significant Changes:**

Updated Waiver Consideration, Table 1 and References

#### I. Waiver Consideration

A history of central nervous system (CNS) infection (e.g., meningitis, encephalitis, meningoencephalitis, brain abscess) is disqualifying for flying duties in the US Air Force according to the Air Force Medical Standards Directory (MSD. Waiver requests may be submitted as soon as the individual is symptom free, cleared by Neurology or Infectious Disease consultants, and has normal studies. Encephalitis and abscess cases may require more prolonged observation due to elevated seizure risk. CNS infections are not disqualifying for OSP duties per the MSD.

Table 1: Waiver potential for meningitis and encephalitis

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation          |
|-------------------|------------------|------------------|-----------------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | Yes                               |
| FC II/III/SWA     | Yes <sup>1</sup> | MAJCOM           | Yes                               |
| ATC/GBO           | Yes <sup>1</sup> | MAJCOM           | At discretion of waiver authority |

Waiver consideration based on amount of residual symptoms and deficits. Encephalitis and non-aseptic meningitis cases may require additional observation due to seizure risk Indefinite waiver recommendation possible in selected cases with complete resolution or minimal non functionally-limiting residua.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

## A. <u>Initial Waiver Request:</u>

- 1. Complete history of event detailing all symptoms, evaluation, treatment, current symptoms and activity level.
- 2. Copies of relevant clinical notes (particularly consultation reports from Neurology and [if obtained] Infectious Disease), diagnostic studies (lumbar puncture results, other lab studies, and EEGs if obtained), imaging reports and copies of images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical, mental status and neurologic examination findings
- 4. Audiogram in cases of encephalitis, meningoencephalitis or bacterial, fungal, or parasitic meningitis occurring within the last 3 years.
- 5. Sleep-deprived EEG in cases of encephalitis.

6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical and neurologic exam findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Aeromedical concerns include the effects of any residual neurologic or cognitive symptoms on operational safety and mission effectiveness, future risk of recurrent infection, and future risk of seizures. Meningitis is an inflammatory process involving the tissues surrounding the central nervous system, while encephalitis involves the brain parenchyma. Some patients have symptoms and signs suggesting involvement of both brain and meninges, blurring the distinction between the two. Acutely, cognitive impairment, obtundation, focal neurological deficits including cranial nerve deficits and hemiparesis, and seizures are significant issues, while residual neurocognitive impairments, movement disorders, and seizures are of future concern. For purposes of aeromedical disposition, aseptic meningitis is defined as no abnormality in brain function (e.g., altered cognitive function, focal neurological deficit), when the CSF findings include a mild pleocytosis (100-1000 cell/mm<sup>3</sup> with either mononuclear or polymorphonuclear cell predominance), negative bacterial smears and cultures, normal to mildly elevated protein concentration, and normal to slightly depressed glucose level, and when the clinical course is relatively short. If there is any alteration of cognitive function, obtundation, focal neurological deficit, or complicated hospital or recovery course, then for purposes of aeromedical waiver that is considered to be no longer simple aseptic meningitis but is in the meningoencephalitis or encephalitis continuum. The prognosis is highly variable depending upon the agent responsible for the meningitis or encephalitis. However, in general, simple aseptic (viral) meningitis has an excellent prognosis, although definitive therapy is still somewhat controversial. More complicated forms of viral meningitis, such as West Nile virus or HIV, as well as meningitis secondary to bacterial, fungal, or parasitic agents do not share the same good prognosis. All forms of encephalitis or meningoencephalitis carry a significant risk of chronic neurocognitive or neurological impairment and seizures, and require additional evaluation and observation prior to waiver consideration. Annegers' study from 1988 indicated a 10% risk of seizures over 20 years for viral encephalitis without early seizures, 22% risk with early seizures, 13% risk for bacterial meningitis with early seizures and only 2.4% risk for bacterial meningitis without early seizures.

Late unprovoked seizures may occur in up to 65% of patients following herpes simplex encephalitis. Other neurological complications may be seen, including a high incidence of neurocognitive and movement disorders in West Nile and Japanese encephalitis. Bacterial brain abscesses carry an increased seizure risk for at least three years post-resolution.

Review of AIMWTS in Dec 2018 showed 104 cases of encephalitis and/or meningitis; 19 FC I/IA, 36 FC II, 2 RPA pilots, 41 FC III, and 6 ATC/GBC. Of the 104, 6 were disqualified (2 FC I and 4 FC III).

| ICD-9 Codes for Meningitis and Encephalitis |   |  |
|---|---|--|
| 047.9                                       | Unspecified viral meningitis                                      |  |
| 320.9                                       | Meningitis due to unspecified bacterium                           |  |
| 322.9                                       | Meningitis, unspecified   |  |
| 323.9                                       | Unspecified cause of encephalitis, myelitis and encephalomyelitis |  |

| ICD-10 C | ICD-10 Codes for Meningitis and Encephalitis    |  |  |
|----------|---|--|--|
| A87.9    | Viral meningitis, unspecified                   |  |  |
| G00.9    | Bacterial meningitis, unspecified               |  |  |
| G03.9    | Meningitis, unspecified                         |  |  |
| B04.90   | Encephalitis and encephalomyelitis, unspecified |  |  |

## IV. Suggested Readings

- 1. Davis LE. Acute bacterial meningitis. Continuum (Minneap Minn) 2018; 24(5):1264-1283.
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#### Mental Health Waiver Guide Checklist (Jan 2019)

Reviewed: Lt Col Kevin F. Heacock (ACS Neuropsychiatry Branch Chief), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col I. David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: New Document

## **Required Period of Clinical Stability**

A period of clinical stability is required after the aviator's "Best Baseline" is achieved. "Best Baseline" is reached when the aviator's Mental Health Provider (MHP) determines the symptoms of the diagnosis are no longer causing clinically significant distress or impairment and the aviator demonstrates adequate function in social, occupational, and other important areas for functioning. Once "Best Baseline" is reached treatment adjustments can still be made, including medication changes, without restarting the period of clinical stability as long as the aviator's levels of distress, impairment, or functioning have not deteriorated to a point which the MHP determines to be clinically significant. Different diagnoses require different lengths of clinical stability prior to requesting a waiver.

- 1 Year—Psychotic Disorders, Somatic Symptoms and Related Disorders, & Eating Disorders
- 6 Months—Mood Disorders, Anxiety, PTSD, & Suicidal Behavior
- **Discretion of Flight Surgeon**—Adjustment Disorder & Other Conditions that May Be a Focus of Clinical Attention requiring waiver
- For aviators with any other psychiatric disorders, please refer to AFI 48-123, Medical Standards Directory (MSD) Section Q: Psychiatry and Mental Health, and ACS Waiver Guides

#### **Required Items for Waiver Package**

- Submit waiver package **30 days BEFORE** the required period of stability is reached to ensure the aviator is evaluated as close to their waiver eligibility as possible.
- Please make every effort to provide **complete documentation**. AHLTA is not reliably accessible at the Aeromedical Consultation Service (ACS) and so the Waiver Package should include a PDF of all Mental Health notes in chronological order.
- If the aviator is **Guard** or **Reserve** and has difficulty accomplishing a required item, please note this in the AeroMedical Summary (AMS).
- A well-written and complete evaluation following the waiver guide's template for mental health evaluations improves the chance for an aeroletter disposition with no need for an expensive week long TDY to ACS for face-to-face evaluation
- All Items are needed for both Initial Waiver Requests and Renewal Waiver Requests.

## 1. Mental Health Evaluation – within 1 month of submission – See Template

- To be accomplished after "Best Baseline" as above.
- The evaluator should be a **doctoral level MHP** with preference for a **Psychiatrist** if the aviator is on **psychotropic medication.**

## 2. Flight Surgeon's AeroMedical Summary (AMS) – See Template

- Utilize the Mental Health Evaluation, and summarize the Flight Surgeon's interview of aviator, Commander Letter, and collateral information (supervisor, spouse, etc.).

# 3. ALL Past Mental Health and Pertinent Medical Records – $\underline{\text{See Authorization}}$ Form

- Military **AND** Civilian records are required (MH records behind "break glass" are needed).
- Records to submit include: outpatient, inpatient, partial hospitalization, intensive outpatient, ADAPT, FAP, detox/rehab, Pre-military if relevant (child mental health care).

#### 4. Commander's Endorsement Letter

- A memo from the aviator's commander supporting their request for waiver and providing insight into the aviator's ability to function effectively at work is very helpful.

## 5. All Pertinent Labs

- Alcohol Use Disorder cases require at least 2 unannounced Carbohydrate-Deficient Transferrin (CDT) studies to demonstrate abstinence.
- **6. Copy of Abstinence Letter -** for Alcohol Use Disorder cases.

## Please feel free to contact the ACS Neuropsychiatry Branch with questions:

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il

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# **Mental Health Evaluation for Aeromedical Summary**

- 1. Date symptoms started. Why then? Comment on context and etiology.
- 2. Initial symptoms and symptoms at their worst.
- 3. How symptoms impacted military and flight duties.
- 4. Date and circumstances of presentation (self-referral, CDE, spouse threatened divorce, etc.).
- 5. Type and length of treatment:

# a. Psychotherapy

- i. Name of Provider (psychologist, social worker)
- ii. Type of therapy (CBT, PE, EMDR, etc.), focus, and core issues
- iii. Total number of sessions from when to when

#### **b.** Medication treatment

- i. Name of Provider (psychiatrist, PCM, FS, PMHNP, PA)
- ii. Medication(s) prescribed, impact, compliance, side effects, and dates
- iii. Current medications

## c. Healthy lifestyle interventions

- i. Premorbid
- ii. Learned and utilized during treatment
- iii. Current utilization for coping and resilience
- 6. Date aviator returned to "Best Baseline" even if still receiving ongoing medication(s) or psychotherapy. Comment on symptom resolution and need for ongoing treatment.
- 7. Changes in screening measures (PHQ-9, GAD-7, PCL-5, etc.) and psychological testing with RAW DATA and interpretation, if administered.
- 8. Review of systems, past medical history, past psychiatric history, family psychiatric history, appropriate developmental history, social history, and substance use (caffeine, smoking, EtOH, etc.).
- 9. Current mental status, level of function at work, in military environment, in family, in personal life, and ability to perform under stress and in operational/aviation setting.
- 10. Comment on aviator's awareness, insight, new skills obtained and used, coping ability, and successes. Comment on how aviator tolerated past and recent stressors (indications of resilience).
- 11. Diagnosis supported by DSM-5 criteria.
- 12. Estimated risk of recurrence, based on DSM-5, patient's history, and evaluator's experience.
- 13. Motivation to return to flying duties.

# Flight Surgeon's AMS Template for Mental Health Waiver

- 1. Summary of presentation, course of illness, and treatment.
- 2. How did symptoms impact military and flight duties?
- 3. Date and circumstances of presentation (self-referral, command-directed, spouse threatened divorce, etc.), and initial mental health treatment.
- 4. Type and length of treatment.
- 5. Date aviator returned to "Best Baseline" even if still receiving ongoing medication(s) or psychotherapy. Comment on symptom resolution and if there is a need for ongoing treatment. Confirm required period of stability has been met for the diagnosis.
- 6. Current mental status, level of function at work, in military environment, in family, in personal life, ability to perform under stress and **capacity to function in stressful aviation/operational settings.**
- 7. Comment on aviator's awareness, insight, new skills obtained and used, coping ability, and successes. Comment on how aviator tolerated past and recent stressors (indications of resilience).
- 8. Diagnosis, supported by DSM-5 criteria.
- 9. Estimated risk of recurrence, based on DSM-5, patient's history, and Flight Surgeon's experience.
- 10. Comment on ability, stability, and motivation to fly (or special duty).
- 11. Discuss Command support.
- 12. Estimated aeromedical risk if aviator is returned to flight status. Address the following:
  - a. Risk of sudden incapacitation
  - b. Risk of subtle performance decrement
  - c. Stability under stress (physiological or emotional)
  - d. Possibility of progression or recurrence
  - e. Need for exotic tests
  - f. Compatibility to perform sustained flight operations in austere environments
- 13. Flight Surgeon's endorsement, consultative question(s), and final recommendations.

| AUTHORIZATION FOR DISCLOSURE OF MEDICAL OR DEM  | NTAL INFORMATION                      |                                    |
|---|---------------------------------------|------------------------------------|
| PRIVACY ACT STATEMENT In accordance with the Privacy Act of 1974 (Public Law 93-579), the replease read it carefully. AUTHORITY: Public Law 104 -191; E.O. 9397 (SSAN); DoD 6025. | • • •                                 | the form and ho w it will be used. |
| <b>PRINCIPAL PURPOSE(S):</b> This form is to provide the Military Tro   | eatment Facility/Dental Treatment F   | Facility/TRICARE Health Plan with  |
| a means to request the use and/or disclosure of an individual's protected <b>ROUTINE USE(S):</b> To any third party or the individual upon authori                                |                                       | dividual for personal use          |
| insurance; continued medical care; school; legal; retirement/separation   |                                       | dividual for. personal use,        |
| <b>DISCLOSURE:</b> Voluntary. Failure to sign the authorization form with This form will not be used for the authorization to disclose alcohol or of                              |                                       |                                    |
| SECTION I - PATIENT DATA  | <u> h </u>                            | (:                                 |
| 1. NAME (Last, First, Middle Initial)   | 2. DATE OF BIRTH (YYYYMMDD)           | 3. SOCIAL SECURITY<br>NUMBER       |
| 4. PERIOD OF TREATMENT: FROM - TO (YYYYMMDD)  | 5. TYPE OF TREATMENT (X o             | ·                                  |
| ALL   | OUTPATIENT INPATI                     | ENT BOTH                           |
| SECTION II - DISCLOSURE   | TO DELEACE ME                         | A DA TUDIUT INICODA (A TUDIU       |
| 6. I AUTHORIZETO:   | TO RELEASE MY                         | PATIENT INFORMATION                |
| a. NAME OF PHYSICIAN, FACILITY, OR TRICARE HEALTH   | b. ADDRESS (Street, City, State of    | and ZIP Code)                      |
| PLAN  |                                       | Wright-Patterson AFB, OH 45433-    |
| Neuropsychiatry Branch - Aeromedical Consultation Service   | 7913                                  |                                    |
| c. TELEPHONE (Include Area Code) (937) 938-2768   | <b>d. FAX</b> (Include Area Code) (93 | 7) 904-8753                        |
| 7. REASON FOR REQUEST/USE OF MEDICAL INFORMATIO   |                                       |                                    |
| PERSONAL USE CONTINUED MEDICAL X INSURANCE CARE   | OTHER (Specify) ACS WAIVER SCHOOL     | PACKAGE                            |
| RETIREMENT/SEPARATIO  | SCHOOL                                |                                    |
| 8. INFORMATION TO BE RELEASED   |                                       |                                    |
| All Mental/Behavioral Health (Sections A-F), ADAPT, FAP, and/or ci records to include, but not limited to: background questionnaires, intak                                       |                                       |                                    |
| scores/reports) OO-45 questionnaires PCL-M innatient records treat  | ment notes (not AHI TA conies) et     |                                    |
| 9. AUTHORIZATION START DATE <u>10. AUTHORIZ</u>   | ATION EXPIRATION                      |                                    |
| (YYYYMMDD) DATE (YYYY) SECTION III - RELEASE AUTHORIZATION  | (MMDD)                                | ACTION COMPLETED                   |
| I understand that:  |                                       |                                    |
| I have the right to revoke this authorization at any time. My revocation  | n must be in writing and provided to  | o the facility where my medical    |
| records are kept or to the TMA Privacy Officer if this is an authorizati  | on for information possessed by the   | TRICARE Health Plan rather than    |
| an MTF or DTF. I am aware that if I later revoke this authorization, the  |                                       |                                    |
| protected information on the basis of this authorization.   |                                       |                                    |
| If I authorize my protected health information to be disclosed to some regulations, then such information may be re-disclosed and would no  |                                       | with federal privacy protection    |
| I have a right to inspect and receive a copy of my own protected health   |                                       | d in accordance with the           |
| requirements of the federal privacy protection regulations found in the   |                                       |                                    |
| The Military Health System (which includes the TRICARE Health Pla   |                                       |                                    |
| TRICARE Health Plan, enrolment in the TRICARE Health Plan or eli  |                                       |                                    |
| 11. SIGNATURE OF PATIENT/PARENT/LEGAL<br>REPRESENTATIVE   | 12. RELATIONSHIP TO PATIENT           | 13. DATE (YYYYMMDD)                |
| NEI NEDENTATIVE   | (If applicable)                       |                                    |
| SECTION IV - FOR STAFF USE ONLY (To be completed only upo   | on receipt of written revocation)     |                                    |
| 14. X IF APPLICABLE: 15. REVOCATION COMPLETED BY  |                                       | <b>16. DATE</b> (YYYYMMDD)         |
| AUTHORIZATION<br>REVOKED  |                                       |                                    |
| INL VOICED  |                                       | i                                  |

#### WAIVER GUIDE

Initial Version: Jan 2016

Supersedes Waiver Guides of Aug 2014 (Mitral Regurgitation), Jul 2014 (Mitral Valve Prolapse),

and Feb 2011 (Misc. Valvular Heart Disorders) By: Dr Dan Van Syoc and Lt Col Steven M. Gore

Reviewed by: Lt Col Eddie D. Davenport, ACS Chief Cardiologist

#### **CONDITION:**

Mitral, Tricuspid, and Pulmonic Valve Disorders (Jan 2016)

#### I. Waiver Consideration.

Per Air Force Instruction, any history of valvular heart disease to include mitral valve prolapse, mitral, pulmonic, and tricuspid valve regurgitation with a severity greater than mild, and any degree of valvular stenosis is disqualifying. ACS evaluation is required for waiver consideration. For most aircrew, moderate to severe mitral regurgitation of any etiology is disqualifying if symptomatic or associated with subnormal ejection fraction. Symptomatic MVP requiring treatment is also disqualifying.

## A. Mitral Regurgitation:

- 1. Moderate MR may be eligible for an unrestricted FC II, FC III, ATC/GBO/SWA waiver.
- 2. Asymptomatic severe MR that does not meet ACC/AHA guideline criteria for surgery may be considered for a waiver restricted to low performance aircraft.
- 3. Asymptomatic severe MR that meets ACC/AHA guideline criteria for surgical repair/replacement and symptomatic severe MR are disqualifying without waiver recommendation.<sup>9</sup>

ACS re-evaluations will typically be performed at 1-3 year intervals, depending on the degree of MR and other associated findings such as cardiac chamber dilation and left ventricular dysfunction. The use of approved ACE inhibitors for afterload reduction is acceptable in aviators with moderate or asymptomatic severe MR. Waivers may be considered after surgery. Refer to the "Valve Surgery – Replacement or Repair" waiver guide. For further details of waiver criteria for MR, see Table 1.

## B. Mitral Valve Prolapse (MVP):

- 1. MVP with MR mild or less in severity is eligible for FC I/IA waiver.
- 2. MVP with MR moderate or less in severity is eligible for unrestricted FC II, ATC/GBO/SWA or FC III waiver.
- 3. MVP with MR that is severe, but asymptomatic, and does not meet ACC/AHA guideline criteria for surgery may be considered for a waiver restricted to low performance aircraft.<sup>9</sup>
- 4. MVP with MR that is either "severe and symptomatic" or "severe and asymptomatic", but meets ACC/AHA guideline criteria for surgical repair or replacement, is disqualifying without waiver recommendation.<sup>2</sup>

ACS re-evaluations will be performed at 1-3 years intervals, depending on the degree of MR and other associated findings such as cardiac chamber dilation and left ventricular dysfunction. The use

of approved ACE inhibitors for afterload reduction is acceptable in aviators with MVP and moderate or asymptomatic severe MR. For further details of waiver criteria for MVP, see Table 2.

#### C. Miscellaneous Heart Valve Disorders:

For retention purposes, severe valve or sub-valvular pulmonic stenosis is disqualifying in addition to most cases of symptomatic mitral stenosis. Table 3 summarizes disposition recommendations for several of these valve disorders. Due to the rarity of these valve disorders in our population, they will also be considered on a case-by-case basis.

Additional findings considered in waiver recommendations, include but are not limited to, normal atrial and ventricular size, normal ventricular function, no prior thromboembolic events, no associated tachydysrhythmias and no symptoms attributable to the specific valve disorder. Waivers may be considered after surgery. Refer to the "Valve Surgery – Replacement or Repair" waiver guide.

| Table 1: Summary of Associated Clinical  Degree of Primary Mitral | Flying Class (FC)              | Waiver            | ACS Review and/or |
|---|--------------------------------|-------------------|-------------------|
| Regurgitation (MR) Graded on                                      | 11,1118 01000 (1 0)            | Potential         | Evaluation        |
| Echocardiogram  |                                | 1 otentiai        | Required          |
| Echocardiogram  |                                | Waiver            | Required          |
|   |                                |                   |                   |
| Trace or wild MD (resumed vericus)                                | EC I/IA/II/CDO                 | Authority         | ACS review        |
| Trace or mild MR (normal variant)                                 | FC I/IA/II/GBO                 | Qualified*<br>N/A | ACS review        |
|   | FC III, ATC/SWA                | Qualified*        | No ACS review     |
|   | 1 0 111, 111 0/0 1111          | N/A               | required          |
| Moderate MR   | FC I/IA                        | No                | ACS review        |
| THOUSE WITH   |                                | AETC              |                   |
|   | FC II/III                      | Yes<br>MAJCOM     | ACS evaluation    |
|   |                                |                   |                   |
|   | ATC/GBO/SWA                    | Yes<br>MAJCOM     | ACS Review        |
| Severe MR – asymptomatic and                                      | FC I/IA                        | No                | ACS review        |
| nonsurgical per guidelines  |                                | AETC              | ACS TEVIEW        |
|   | FC IIA only                    | Maybe<br>AFMSA    | ACS evaluation    |
|   | GBO                            | Maybe<br>MAJCOM   | ACS evaluation    |
|   | FC IIIC (low performance only) | Maybe<br>AFMRA    | ACS evaluation    |
|   | ATC/SWA                        | Yes<br>MAJCOM     | ACS evaluation    |
| Severe MR – symptomatic or surgical per guidelines &              | FC I/IA                        | No<br>AETC        | ACS review        |
|   | FC II/RPA Pilot/III            | No<br>AFMRA       | ACS review        |
|   | ATC/GBO/SWA <sup>&amp;</sup>   | Maybe<br>AFMRA    | ACS evaluation    |

<sup>\*</sup>Qualified means no waiver required, however, for FC I/IA/II/RPA Pilot individuals, echos read locally as trace or mild MR require ACS review via the ECG Library. The report and a CD/videotape copy are required for confirmation and to exclude underlying pathology such as MVP.

<sup>\*\*</sup>No waiver required if member asymptomatic and has a normal ejection fraction.

<sup>&</sup>amp; Successful mitral repair with preservation of ejection fraction, no need for anticoagulants or anti-arrhythmics may be waived if exercise tolerance is normal, but DAWG review (with MEB/IRILO as appropriate) must precede surgery.

**Table 2: Waiver Potential for MVP** 

| MVP and Associated                        | Flying Class          | Waiver Potential | Required ACS Review           |
|---|-----------------------|------------------|-------------------------------|
| Levels of Mitral                          | 1 1) 111g 0 1000      | Waiver           | and/or ACS Evaluation         |
| Regurgitation (MR)                        |                       | Authority†       |                               |
| Documented by                             |                       |                  |                               |
| Echocardiogram                            |                       |                  |                               |
| MVP with mild or less MR                  | FC I /IA              | Yes              | ACS evaluation                |
|   |                       | AETC             |                               |
|   |                       |                  |                               |
|   | FC II/III             | Yes*             | ACS evaluation                |
|   |                       | MAJCOM           |                               |
|   | 4 mg/gp 0 2gyyy 4     |                  | . ~~                          |
|   | ATC/GBO?SWA           | Yes              | ACS review                    |
| MVP with moderate MR                      | FC I/IA               | AFGSC            | ACS review                    |
| MVP with moderate MR                      | FC I/IA               | No<br>AETC       | ACS review                    |
|   |                       | AEIC             |                               |
|   | FC II//III            | Yes*             | ACS evaluation                |
|   |                       | MAJCOM           | Ties evaluation               |
|   |                       |                  |                               |
|   |                       |                  |                               |
|   | ATC/GBO/SWA           | Yes              | ACS review                    |
|   |                       | MAJCOM           |                               |
| MVP with severe MR -                      | FC I/IA               | No               | ACS review                    |
| asymptomatic and                          |                       | AETC             |                               |
| nonsurgical MR per guidelines             | FC IIA only           | Maybe*           | ACS evaluation                |
| guidennes                                 | FC IIA OIIIy          | AFMSAAFMRA       | ACS evaluation                |
|   |                       |                  |                               |
|   | FC IIIC (low          | Maybe*           | ACS evaluation                |
|   | performance           | AFMSA            |                               |
|   | only)                 |                  |                               |
|   |                       |                  |                               |
|   | ATC/GBO/SWA           | Maybe            | ACS review                    |
| MVD solds are ND                          | EC I/IA               | MAJCOM           | A CC                          |
| MVP with severe MR –                      | FC I/IA               | No<br>AETC       | ACS review                    |
| symptomatic or surgical MR per guidelines |                       | ACIC             |                               |
| per guidennes                             | FC II//III            | No               | ACS review                    |
|   |                       | MAJCOM           |                               |
|   |                       |                  |                               |
|   | ATC/GBO/SWA           | Maybe            | ACS review                    |
|   |                       | MAJCOM           |                               |
| MVP: clinical (auscultation)              | FC I/IA/II/III        | Yes              | After 3 ACS                   |
| only without a positive echo              | ATC/GBO/SWA           | MAJCOM           | evaluations/reviews without a |
|   |                       |                  | positive echo, an indefinite  |
|   | (individuale unlikely |                  | waiver is recommended         |

<sup>\*</sup> Waiver in untrained FC II and III individuals unlikely.

Table 3: Summary of Associated Clinical Conditions and ACS Requirements

| Table 3: Summary of Associat  Type and Degree of | Flying Class              | Waiver Potential | ACS Review/Evaluation            |
|--|---------------------------|------------------|----------------------------------|
| Valvular Disease                                 | rlying Class              | waiver roteittar | Required                         |
| Graded on  |                           | Waiver Authority | Required                         |
|  |                           | waiver Aumority  |                                  |
| Echocardiogram                                   | EC I/I A                  | O1:6:1           | ECC Library and                  |
| Trace or mild PI and TR                          | FC I/IA                   | Qualified<br>N/A | ECG Library review               |
|  | FC II/III                 | Qualified        | FC II - ECG Library review,      |
|  | ATC/GBO/SWA               | N/A              | FC III, ATC/GBO/SWA not required |
| Moderate PI and TR                               | FC I/IA                   | Maybe<br>AETC    | ACS evaluation                   |
|  | FC II//III<br>ATC/GBO/SWA | Maybe<br>MAJCOM  | ACS evaluation#                  |
| Severe PI and TR –                               | FC I/IA                   | No               | ACS review                       |
| asymptomatic and                                 |                           | AETC             |                                  |
| nonsurgical per                                  |                           |                  |                                  |
| guidelines                                       | FC IIA only               | Maybe*<br>AFMRA  | ACS evaluation                   |
|  | FC IIIC (low              | Maybe*<br>AFMRA  | ACS evaluation                   |
|  | performance only)         | Mayba*           |                                  |
|  | ATC/GBO/SWA               | Maybe*<br>MAJCOM | ACS evaluation#                  |
| Consonital mild DC                               |                           | Yes              | ACS evaluation  ACS evaluation   |
| Congenital mild PS                               | FC I/IA                   | AETC             | ACS evaluation                   |
|  | FC II/III                 | Yes              | ACS evaluation                   |
|  | ATC/GB)/SWA               | MAJCOM           | 71CD Cvariation                  |
| Any degree of mitral or                          | FC I/IA                   | No               | ACS review                       |
| tricuspid valve stenosis                         |                           | AETC             | 11CD ICVICW                      |
|  | FC II RPA Pilot//III      | No<br>MAJCOM     | ACS review                       |
|  | ATC/GBC<br>MOD            | Maybe<br>MAJCOM  | ACS review                       |

<sup>\*</sup>Waiver for untrained FC II and III individuals unlikely.

AIMWTS search in Jan 2016 revealed 304 Air Force members with a waiver disposition for mitral valve, tricuspid valve, or pulmonic valve disorders. There were 41 disqualifications (one was

<sup>#</sup>ACS evaluation not required for ATC/GBC personnel and waiver may be recommended based on ACS review.

eventually given an ETP – FC III). Breakdown of the cases revealed 19 FC I/IA cases (4 disqualified), 162 FC II cases (13 disqualified), 113 FC III cases (21 disqualified), 5 ATC/GBC cases (1 disqualified), and 5 MOD cases (2 disqualified). Approximately 50% of the disqualified cases were due in part to the valvular disease.

## II. Information Required for Waiver Submission.

ACS review/evaluation is required for diagnosis confirmation and aeromedical disposition. The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

ACS review/evaluation is required at least once for all classes of flying duties for moderate or severe MR with waiver renewals recommended based on local studies. No additional studies are routinely required prior to ACS review/evaluation. If the treating physician deems it clinically necessary to perform additional studies, it is required that all studies be forwarded to the ACS for review. There is no minimum required nonflying observation period for ACS review/evaluation.

For <u>initial</u> ACS evaluation the aeromedical summary should contain the following information:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. Complete history and physical examination to include detailed description of symptoms, medications, activity level and CAD risk factors (positive and negative).
- C. Formal report and complete tracings (videotape or CD) of the echo documenting the findings. (Notes 1 and 2)
- D. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. holter, treadmill, stress echocardiogram). (Notes 1 and 2)
- E. Additional local cardiac testing is not routinely required, but may be requested on a case by case basis.
- F. Medical evaluation board (MEB) reports and narrative if applicable.

For <u>follow-up</u> ACS evaluations (re-evaluations) the aeromedical summary should contain the following information:

- A. Complete history and physical examination to include detailed description of symptoms, medications, activity level, and interval history
- B. All applicable labs and imaging tests as required in the initial aeromedical summary.
- C. Local follow-up cardiac testing is not routinely required prior to ACS re-evaluation. If requested for individual cases, it will have been specified in the report of the previous ACS evaluation.
- D. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. holter, treadmill, stress echocardiogram). (Notes 1 and 2)

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI, Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

For expediting the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in the aeromedical summary when studies were sent to ACS.

#### III. Overview.

This waiver guide will combine three previous guides; mitral regurgitation, mitral valve prolapse, and miscellaneous valve disorders, which comprises disorders of the tricuspid and pulmonary valves as well as mitral stenosis.

A. <u>Mitral Regurgitation</u> - Abnormalities of the mitral valve annulus, the valve leaflets, the chordae tendinae, or the papillary muscles can cause mitral regurgitation (MR). In assessing a patient with mitral regurgitation, it is important to distinguish between primary (degenerative) MR or secondary (functional) MR. In primary MR, the pathology of ≥1 of the components of the valve (leaflets, chordae tendinae, papillary muscles, annulus) causes valve incompetence with systolic regurgitation of blood from the left ventricle to the left atrium. Younger populations usually present with severe myxomatous degeneration with gross redundancy of both the anterior and posterior leaflets and chordal apparatus. Older populations present with fibroelastic deficiency in which lack of connective tissue leads to chordal rupture.

In the United States and much of the Western world, the most common cause of MR is mitral valve prolapse (MVP), accounting for as much as one-half to two-thirds of cases. In the aircrew population, clinically significant MR is also most commonly associated with MVP/myxomatous mitral valve disease. Other causes of primary MR include rheumatic heart disease, infective endocarditis, collagen vascular disease, and cleft mitral valve and radiation heart disease. Causes of secondary MR include ischemic and idiopathic myocardial disease leading to a dilated cardiomyopathy.<sup>1,2</sup> Aeromedical considerations for all etiologies of MR will be addressed by the underlying disease process in this waiver guide. Symptom manifestation depends on the etiology and severity of MR. Moderate or less MR should not cause symptoms. Symptoms due to chronic MR are related to progressive volume overload resulting in pulmonary congestion and left ventricular dysfunction. Symptoms of severe MR include reduced exercise tolerance, chronic weakness, fatigability, exertional dyspnea, dyspnea at rest, and orthopnea. However, some subjects with severe MR and associated left ventricular dysfunction may be asymptomatic, with symptom onset being insidious and not appreciated by the patient. A careful history is important to elicit subtle symptoms or lifestyle changes due to the patient "slowing down" or "not being in shape". Atrial fibrillation may be a resultant complication associated with severe MR.<sup>1,2</sup>

In the aircrew population, MR is typically diagnosed by an echocardiogram (echo) ordered for murmur evaluation or for a variety of other clinical or aeromedical indications, such as an abnormal electrocardiogram. MR is graded on echo as trace, mild, moderate or severe. MR graded on echo as trace or mild is considered to be a normal variant (not disqualifying) and no waiver is required.

For FC I/IA/II/RPA Pilot individuals, echocardiogram studies read locally as trace or mild MR require Aeromedical Consultation Service (ACS) review via the ECG Library. The formal report and a CD/videotape copy are required to confirm the local read and to exclude underlying pathology such as MVP. ACS review for trace to mild MR is optional for FC III, and can be requested by the local flight surgeon or the waiver authority if desired. A waiver is required for all classes of flying duties when MR is graded moderate or severe.

B. Mitral Valve Prolapse (MVP) - The prevalence of MVP is reported to be 2-5% in the general U.S. population. The prevalence of MVP utilizing data from the USAF database of Medical Flight Screening (MFS) echocardiograms performed on pilot training candidates, was about 0.5% in males and females. The lower prevalence seen in the USAF database may be due to the young age of this population and elimination of some of the more obvious cases during the examination process. MVP may be diagnosed or suggested by the typical auscultatory findings of a mid-systolic click with or without a late systolic murmur, but is more typically diagnosed by echocardiography (echo) evaluation. The current echocardiographic definition of MVP is billowing of any portion of the mitral leaflets  $\geq 2$  mm above the annular plane in a long axis (parasternal or apical 3-chamber) view. Echo criteria have evolved over the years, but current standards are widely accepted and unlikely to significantly change in the near future. These criteria have been followed by the ACS for over a decade since their earliest acceptance by the academic cardiology community, but many civilian cardiologists may not adhere to the currently defined strict criteria. Therefore, verification of a local MVP diagnosis needs to be completed by the ACS in all cases.

Historically, there have been reports of a possible association between panic disorder or social anxiety disorder and MVP. The purported relationship between these conditions is most likely a matter of chance and the result of a confluence of factors. Additionally, other symptoms to include palpitations, dyspnea, exercise intolerance, dizziness, numbness or tingling, skeletal abnormalities, and abnormal resting and exercise electrocardiograms have been attributed to MVP. Recent investigations into these associations have not conclusively shown a direct link between and reassurance about the benign nature of MVP is usually enough to reduce the severity of associated symptoms. 8

Progressive mitral regurgitation is one of the primary clinical and aeromedical concerns with MVP due to morphologic changes of the valve leaflets and chordae tendinae. In the aircrew population, clinically significant MR is commonly associated with mitral valve prolapse/myxomatous mitral valve disease. Given the progression rates, all MVP requires waiver for flight duties even if no associated regurgitation or stenosis. Despite some risk of progression to severe MR, most aviators with MVP can be reassured the condition (and associated MR) is not life threatening.<sup>6</sup>

#### C. Misc. Valvular Heart Disorders

- 1. Regurgitation/insufficiency of the tricuspid (TR) and pulmonic (PI) valves
- 2. Mitral stenosis (MS), Tricuspid stenosis (TS) and Pulmonic stenosis (PS)

These disorders are commonly asymptomatic and thus found incidentally during echocardiography evaluation for other reasons. The natural history and progression of disease depends on the underlying cause. <sup>9, 10</sup> These valve disorders will be rarely, if ever, seen in our aviator population. The most common pathology seen in the AIMWTS database search is TR with the majority being graded as trace to mild in severity, thus considered a normal variant. <sup>1, 2</sup>

In the aircrew population, regurgitation/insufficiency or stenosis of these cardiac valves will typically be diagnosed by an echocardiogram (echo) ordered for cardiac murmur evaluation or a variety of other clinical or aeromedical indications, such as an abnormal electrocardiogram. As with mitral regurgitation, tricuspid and pulmonic regurgitation is graded as trace, mild, moderate or severe. In the absence of morphologic valve pathology, tricuspid and pulmonic valve regurgitation graded as trace or mild are considered normal variants. They are not disqualifying and a waiver is not required. Conversely, any degree of mitral, tricuspid or pulmonary valve stenosis is considered abnormal.<sup>1,2</sup>

For FC I/IA/II/RPA Pilot individuals, echocardiograms interpreted locally as trace or mild TR and/or PI (i.e. normal variants) require review and confirmation via the Aeromedical Consultation Service (ACS) ECG Library. The formal report and a CD/videotape copy are required for confirmation in order to exclude underlying pathology such as valve prolapse. If ACS ECG Library review confirms trace or mild PI and/or TR with no valve pathology, a letter to this affect will be sent and incorporated into the patient's medical record. The individual is considered medically qualified and no waiver or further work-up is required. If ACS ECG Library review determines TR and/or PI severity is worse than trace or mild, a letter will be sent directing the need for a waiver. ACS ECG Library review of trace to mild TR and/or PI is optional for FC III, but may be requested by the local flight surgeon or the waiver authority if desired. Locally interpreted echocardiograms with moderate or greater TR and/or PI and any degree of mitral, tricuspid, or pulmonic stenosis, will require ACS evaluation. The formal report and a CD/videotape copy are required for confirmation.

In early 2007, the American Heart Association published new infective endocarditis guidelines that are dramatically different from past recommendations.<sup>3</sup> Endocarditis prophylaxis is recommended only for specified high risk groups, and only for specified dental procedures, respiratory tract procedures, and procedures on infected skin, skin structures or musculoskeletal tissue. The high risk group was limited to prosthetic cardiac valves, previous endocarditis, select congenital heart conditions and cardiac transplant patients with valvulopathy. Prophylaxis was no longer recommended for gastrointestinal or genitourinary procedures. Conditions commonly seen by most aerospace medicine practitioners were not included in the list of high risk conditions. Common conditions no longer recommended for endocarditis prophylaxis included, but are not limited to, mitral valve prolapse, bicuspid aortic valve, mitral or aortic regurgitation with normal valve morphology and uncorrected small defects of the atrial and ventricular septum.

#### IV. Aeromedical Concerns.

A. <u>Mitral Regurgitation and Mitral Valve Prolapse (MVP)</u>: Two categories of aeromedical events must be considered with MVP and moderate or severe MR. First, events which might occur abruptly and impact flying performance include sudden cardiac death, cerebral ischemic events, syncope, presyncope and sustained supraventricular and ventricular tachydysrhythmias. Second, progression to severe MR, requirement for surgical mitral valve repair or replacement, other thromboembolic events and non-sustained tachydysrhythmias are of aeromedical concern.

ACS experience with moderate and severe primary MR is very limited. However, a review of the ACS experience with 404 trained aviators with MVP is applicable. This review yielded event rates of 1.5% per year for all aeromedical endpoints examined. Most of these could be readily

tracked by serial evaluations and represented a low risk for sudden incapacitation. For events which might suddenly impact flying performance, the rate was only 0.3% per year. The majority of the MVP subjects in this review had less than moderate or severe MR. The primary aeromedical concern of moderate to severe MR would be the development of symptoms and progression to severe MR that meets guideline criteria for surgical repair or replacement of the mitral valve. Fortunately, surgical criteria can be tracked and followed by serial echocardiogram studies and patients who are followed closely will usually be identified before symptom onset and elective surgery can be scheduled.

In general, exercise produces no significant change or a mild decrease in MR because of reduced systemic vascular resistance. However, patients with elevation of heart rate or blood pressure as a result of static or isometric exercise may manifest increased MR and pulmonary capillary pressures. Static exercises that increase arterial pressure are potentially deleterious. Ejection fraction usually does not change or decreases slightly with exercise. However, the ejection fraction response may be completely normal in younger asymptomatic subjects. These latter concerns may be more theoretical than clinically relevant, but nonetheless result in a recommendation for restricting static exercise in competitive athletes with significant MR.<sup>9</sup> In the aeromedical environment, "pulling Gs" is a similar situation and reduced +Gz tolerance and +Gz-induced tachydysrhythmias are of concern with severe MR. In an ACS MVP database review, 95 aviators had a monitored centrifuge assessment. Non-sustained supraventricular tachycardia and non-sustained ventricular tachycardia each occurred in one individual (1/95, 1%). G-loss of consciousness occurred in two individuals (2/95, 2%) without an associated cardiac dysrhythmia in either case. These occurrences are less than previously reported for apparently healthy centrifuge subjects or trainees. <sup>13</sup> Notably, a slight reduction in +Gz tolerance has been reported for MVP, but was operationally nonsignificant. 14-17 Therefore, monitored centrifuge assessment is no longer required for MVP or primary MR, but may be used on a case by case basis as deemed necessary by the ACS. An unrestricted waiver may be considered for moderate MR, but waiver consideration for severe MR is limited to low performance aircraft.

Medications that reduce afterload, such as ACE inhibitors, have a documented clinical benefit in acute MR and chronic aortic insufficiency. However, no studies have shown a clinical benefit for MVP or chronic primary MR. Although some studies have shown hemodynamic improvement and relief of symptoms, medication use has not been shown to delay the need for surgery or improve surgical outcome, in contrast to that seen for severe aortic insufficiency. Use of afterload reducing medications in symptomatic MR is appropriate, but at this stage, the aviator should be disqualified and aeromedical disposition should be secondary to clinical disposition regarding proper timing of valve surgery. The use of approved ACE inhibitors is acceptable in aviators with asymptomatic moderate or severe MR.<sup>1</sup>

B. <u>Miscellaneous Heart Valve Disorders</u>: In general, aeromedical concerns for these various valve disorders include progression of the regurgitation and/or stenosis, requirement for surgical or catheter-based valve repair or replacement, underlying or associated disease processes, thromboembolism and arrhythmias. <sup>1, 2, 9, 10</sup>

| ICD-9 codes for mitral valve and misc. valve disorder |   |  |
|---|---|--|
| 394.0   | Mitral Stenosis                                       |  |
| 394.1   | Rheumatic mitral insufficiency                        |  |
| 394.9   | Other and unspecified mitral valve disease            |  |
| 397.0   | Diseases of the Tricuspid Valve                       |  |
| 397.1   | Rheumatic diseases of the Pulmonary Valve             |  |
| 424.0   | Mitral valve disorders                                |  |
| 424.2   | Tricuspid Valve disorders, specified as non-rheumatic |  |
| 424.3   | Pulmonary Valve disorders                             |  |
| 742.02  | Congenital Pulmonary Stenosis                         |  |
| 746.02  | Stenosis of Pulmonary Valve                           |  |
| 746.6   | Congenital mitral insufficiency                       |  |

| ICD-10 codes for mitral valve and misc. valve disorder |  |  |
|--|--|--|
| I05.0  | Rheumatic Mitral Stenosis                    |  |
| I05.1  | Rheumatic mitral insufficiency               |  |
| I07.8  | Other rheumatic tricuspid valve diseases     |  |
| I09.89   | Other specified rheumatic heart diseases     |  |
| I34.0  | Nonrheumatic mitral (valve) insufficiency    |  |
| I34.1  | Nonrheumatic mitral (valve) prolapse         |  |
| I34.8  | Other nonrheumatic mitral valve disorders    |  |
| I36.9  | Other nonrheumatic tricuspid valve disorders |  |
| I37.7  | Other nonrheumatic pulmonary valve disorders |  |
| Q23.2  | Congenital mitral stenosis                   |  |
| Q23.3  | Congenital mitral insufficiency              |  |

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# **Mood Disorders: Depressive, Bipolar and Related Disorders (Sep 2019)**

Reviewed: Lt Col Kevin F. Heacock (ACS Neuropsychiatry Branch Chief), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

# **Significant Changes:**

Restructuring of Waiver Guide, Anti-depressant management, AIMWTS review

#### I. Waiver Consideration

Mood disorders are disqualifying for all flying classes to include ATC/GBO and SWA duties. Untreated or undertreated mood disorders may have potentially disastrous consequences. To mitigate such outcomes, the FAA, Transport Canada, Australia, and the US Army have policies allowing selected aviators to fly while on SSRI's. The USAF followed suit in 2013 allowing select FC II/III personnel to be considered for waivers on antidepressants. After 5 years of observation, in 2018 the USAF allowed all aviators, including single seat and B-2 pilots, to be considered for waivers on the following monotherapies:

- 1. Sertraline (Zoloft®) up to 200 mg/day
- 2. Citalopram (Celexa®) up to 40 mg/day
- 3. Escitalopram (Lexapro®) up to 20 mg/day
- 4. Bupropion (Wellbutrin®) SR or XL up to 400 mg/day or 450 mg/day, respectively.

The aviator on a maintenance antidepressant (only one aeromedically approved medication allowed) needs to be on the medication and remain clinically asymptomatic for at least 6 months before waiver consideration. The dose of the medication can be adjusted to maximize treatment and/or limit side effects without restarting this 6-month period as long as the aviator's symptoms remain stable. If a psychotropic medication is ever adjusted in dose or discontinued in an aviator, two weeks of observation should occur before considering resuming full flight duties to assure no adverse/unexpected side effects or return of symptoms occur. If symptoms return after discontinuing treatment, a return to, or enhancement of, psychotherapy, healthy lifestyle interventions, and/or antidepressant medication for maintenance treatment should be considered.

Waivers are not considered for FCI personnel on antidepressants and are limited to FCII, FCIII, ATC, GBO, and SWA. All FCII, FCIII, and SWA listed (Boom Operator, Flight Engineer, Loadmaster, Aerial Gunner, Combat Control, Pararescue Jumper, Tactical Air Control Party) require ACS review or evaluation and AFMRA waiver. For all other FCIII AFSCs, ACS review is encouraged, and MAJCOM dispositions the waiver.

MOD personnel may be permitted to perform their duty while on certain psychotropic medications listed on the Approved Space and Missile Operator Medications list, but a waiver is typically required.

To be considered for waiver, a mental health evaluation with accurate diagnosis per the Diagnostic and Statistical Manual (DSM) is the vital first step. USAF psychology and/or psychiatry specialists familiar with aeromedical standards are the preferred choice for evaluation and potential development of the treatment plan.

# **DEPRESSIVE DISORDERS**

If the diagnostic criteria for Major Depressive Disorder (MDD), Persistent Depressive Disorder (Dysthymia), or Unspecified Depressive Disorder are met, the aviator is disqualified. A history of two episodes of MDD increases the probability of recurrence to approximately 70%. Therefore, recurrent episodes of depressive disorders are generally disqualifying and not waiverable because of the likelihood of a continually emerging pattern of depressive symptoms negatively affecting overall performance and reliability.

If the diagnosis of a depressive disorder is established, then grounding the aviator is necessary to allow optimal treatment to be initiated. Psychotherapy, healthy lifestyle interventions, and/or psychotropic medications may be utilized as treatment options until depressive symptoms are fully resolved. This is an important goal because partial resolution of symptoms may lead to long-term psychiatric morbidity. Typically, antidepressants are continued for 6-12 months after full resolution of depressive symptoms in order to prevent abrupt relapse after medication cessation. Psychotherapy may be continued after symptom resolution to bolster resiliency and coping mechanisms. A waiver may be considered after 6 months of demonstrated stability (i.e., aviator is back to best baseline functioning). Therefore, it is important for the mental health professional to designate the date of full resolution of symptoms. It is from that date that 6 months of stability should be measured for potential waiver, regardless of ongoing psychotropic medication and/or psychotherapy in pursuit of optimal therapeutic benefit.

# **BIPOLAR and RELATED DISORDERS**

Any aviator with any of the bipolar disorders is permanently disqualified and not eligible for waiver due to the risk of recurrence, the presenting symptoms of loss of insight, tenuous reality-testing, and the unlikelihood of self-referral, poor judgment and poor treatment compliance. The treatment options for bipolar disorders (mood stabilizers and atypical antipsychotics) are not aeromedically-approved for aviators and are not waiverable. In such cases, a medical evaluation board (MEB) should be held to determine fitness for general duty and retention. There is a 29% risk of developing bipolar disorder if both parents are diagnosed with bipolar disorder. Therefore, a family history of a bipolar disorder in both parents is disqualifying for FCI/IA, but can be considered for a waiver after a very thorough mental health evaluation.

Table 1: Waiver potential for mood disorders

| Flying Class (FC) Condition Waiver I |                           | Waiver Potential      |
|--------------------------------------|---------------------------|-----------------------|
|                                      |                           | Waiver Authority      |
| I/IA                                 | Family history of bipolar | Maybe <sup>1</sup>    |
|                                      | disorder (both parents)   | AETC                  |
|                                      | Bipolar disorders         | No                    |
|                                      |                           | AETC                  |
|                                      | Depressive disorders      | Maybe <sup>2</sup>    |
|                                      |                           | AETC                  |
| II/III                               | Bipolar disorders         | No                    |
| ATC/GBO<br>SWA                       |                           | AFMSA                 |
|                                      | Major Depressive Disorder | Maybe <sup>2, 3</sup> |
|                                      | (MDD), single episode     | MAJCOM <sup>4</sup>   |
|                                      | MDD, recurrent episodes   | No                    |
|                                      |                           | MAJCOM <sup>4</sup>   |
|                                      | Persistent Depressive     | Maybe <sup>2, 3</sup> |
|                                      | Disorder (Dysthymia)      | $MAJCOM^4$            |

<sup>1.</sup> Waiver may be considered after thorough psych evaluation of the applicant

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

### A. Initial Waiver Request:

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

#### B. Renewal Waiver Request:

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

<sup>2.</sup> For all UNTRAINED individuals (FC I/IA, FC II/III, and ATC/GBO/SWA), a waiver is NOT considered if they are currently taking an antidepressant. A waiver is considered after depression is completely resolved and medications and psychotherapy have been discontinued for a minimum of 2 years..

<sup>3.</sup> For all TRAINED personnel (FCII/III and ATC/GBO/SWA), a waiver is considered after depression is completely resolved and stability, on or off medication, has been demonstrated for 6 months.

<sup>4.</sup> If categorical waiver (FC IIC or FC IIIC) is required due to medication requirements, then AFMRA is the waiver authority. If the aviator does not meet retention standards per the MSD, then AFMRA is the waiver authority.

Please feel free to contact the ACS Neuropsychiatry Branch with questions:

ACS Aerospace Medicine Branch, USAFSAM/FECA

c/o Neuropsychiatry Branch <u>USAFSAM.FE.PsychiatryMailbox@us.af.mil</u>

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#### III. Aeromedical Concerns

Mood disorders can be associated with a variety of cognitive, emotional, and behavioral symptoms, including depressed mood, impaired judgement, slowed information processing speed, impaired memory and/or attention and concentration, inflated self-esteem or grandiosity, disturbances in energy and sleep, significant weight loss or gain, psychomotor agitation or retardation, fatigue, distractibility, flight of ideas, inappropriate guilt, indecisiveness, suicidal ideation, and excessive involvement in pleasurable activities that have a high potential for undesirable consequences (e.g., spending sprees, promiscuity, substance abuse). These cognitive, emotional, and behavioral difficulties can lead to observable as well as subtle changes in functioning that negatively affect performance under physically and psychological taxing conditions. As a result, mood disorders, as well as an elevated risk of recurrence for such conditions, are incompatible with aviation safety and flying duties.

Many aviators struggle with depressive disorders. Numerous emotional and behavioral manifestations of depression can impair an aviator's cognitive abilities (e.g. ability to focus, sustain attention and concentration, working and general memory, psychomotor coordination, reasoning, spatial judgement, and reaction time) as well as social functioning (e.g., social isolation and withdrawal, increased irritability/agitation). Some of the more severe symptoms of depression, such as suicidal ideation and impaired reality testing, may be acutely disabling. Furthermore, depression often coexists with anxiety and psychosomatic complaints, as well as substance abuse.

There are aeromedical concerns with the use of psychotropic medications for treatment as well. All psychotropic medications have potentially undesirable or dangerous side effects. Common side effects of antidepressants include nausea, vomiting, diarrhea, insomnia, jitteriness, tremor, agitation, restlessness, perspiration, dizziness, and headaches.

AIMWTS review in Sep 2019 for the diagnoses of major depression and bipolar disease resulted in 241 cases since 1 Jan 2014. Of that total, 130 were disqualified. Breakdown of the review revealed 14 FC I/IA cases (11 disqualified), 38 FC II cases (13 disqualified), 7 RPA pilot cases (6 disqualified), 115 FC III cases (57 disqualified), 43 ATC/GBC cases (30 disqualified), 14 MOD cases (6 disqualified), and 10 SWA cases (7 disqualified).

| ICD-9 codes for mood disorders |  |  |
|--------------------------------|--|--|
| 296.2                          | Major depressive disorder, first episode   |  |
| 296.3                          | Major depressive disorder, recurrent       |  |
| 300.4                          | Persistent depressive disorder (dysthymia) |  |
| 311                            | Unspecified depressive disorder            |  |
| 296.xx                         | Bipolar I disorder                         |  |
| 296.89                         | Bipolar II disorder                        |  |
| 301.13                         | Cyclothymic disorder                       |  |
| 296.80                         | Unspecified bipolar and related disorders  |  |

| ICD-10 codes for mood disorders |  |  |
|---------------------------------|--|--|
| F32.9                           | Major depressive disorder, single episode, unspecified |  |
| F33.9                           | Major depressive disorder, recurrent, unspecified      |  |
| F34.1                           | Dysthymic disorder                                     |  |
| F31.9                           | Bipolar disorder, unspecified                          |  |
| F31.81                          | Bipolar II disorder                                    |  |
| F34.0                           | Cyclothymic disorder                                   |  |

# **IV. Suggested Readings**

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### **Motion Sickness (Jul 2019)**

Reviewed: Maj David Leary (RAM 20); Dr. Dan Van Syoc (ACS Waiver Guide coordinator); Maj Daniel Catrambone and Capt Adam Lohn (USAF physiologists: and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updates in accordance with newest MSD (1 Mar 19), AETCI 36-2205V1 (16 Feb 16), and AETCI 48-102 (7 Mar 19).

#### I. Waiver Consideration

Motion sickness experienced in aircraft, automobiles, or watercraft after the age of 12 with any significant frequency in applicants for undergraduate pilot training (UPT), undergraduate navigator training (UNT) (FC I/IA), and Special Warfare training requires a waiver. Any history of motion sickness occurring before age 12 does not specifically require a waiver, but does require exploration. A thorough history of motion sickness should be discussed in the aeromedical summary. Motion sickness is *not* disqualifying for FC II or FC III personnel, unless there is medical evidence of organic or psychiatric pathology.

UPT (FC I) and UNT (FC IA) trainees who have intractable airsickness after completing the Airsickness Management Program (AMP) are usually handled administratively because they are unable to meet syllabus requirements or they demonstrated "lack of adaptability" to the flying environment. However, non-rated student fliers (FC III) enrolled in flying courses, who have intractable airsickness after completing the AMP, are usually medically disqualified and generally are not eligible for waiver. Final determination of medical qualification in these cases is by the MAJCOM/SG.

Rated aircrew (FC II) with intractable airsickness who do not become asymptomatic after repeated exposures to the flying environment and who fail desensitization training are dealt with administratively through a Flying Evaluation Board (FEB). Prior to convening a board, these cases reviewed by the MAJCOM/SG to rule out an organic or psychiatric etiology. Many times these individuals are reassigned to their previous platform.

Airsickness requiring pharmacologic therapy beyond the AMP is disqualifying and not eligible for waiver.

**Table 1: Waiver potential for Motion Sickness** 

| Flying Class<br>(FC)       | Disease/Condition  | Waiver Authority<br>Waiver Potential | ACS<br>Review/<br>Evaluation |
|----------------------------|--|--------------------------------------|------------------------------|
| FC I/IA<br>SWA (initial)   | History of Motion Sickness age >12 yrs. <sup>1</sup>                   | AETC<br>Maybe                        | No                           |
|                            | Motion Sickness during UPT/UNT/Special Warfare training                | AETC<br>Maybe                        | No                           |
| FC II/III<br>SWA (trained) | History of Motion Sickness   | N/A                                  | N/A                          |
|                            | Motion Sickness during initial training                                | MAJCOM<br>Maybe                      | No                           |
|                            | Airsickness with medical evidence of organic or psychiatric pathology. | MAJCOM<br>Maybe                      | Maybe                        |
|                            | History of Motion Sickness   | N/A                                  | N/A                          |
| ATC/GBO                    | Motion Sickness during training  | N/A                                  | N/A                          |
|                            | Airsickness with medical evidence of                                   |                                      |                              |
|                            | organic or psychiatric pathology.                                      | N/A                                  | N/A                          |

<sup>1.</sup> History of motion sickness before the age of 12 that has resolved does not require a waiver, but should be completely explored.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. Childhood and adolescent history of any type of motion sickness
  - b. History of vestibular disorders
  - c. Motion sickness risk factors
  - d. Motion sickness in Air Force

- i. Treatments attempted with results
- ii. Any and all medications attempted with results
- iii. How symptoms affect mission and/or training
- 2. Any specific diagnostic tests performed, before and after treatment (as indicated).
- 3. If vision was involved, Optometry or Ophthalmology consultation, to include all tests
- 4. Current physical examination findings (specific focus on CNS and ENT exams)
- 5. Any other pertinent information.
  - a. Include discussion and results from any Airsickness Management Program (AMP) training.
  - b. Include a statement from the aerospace physiologist regarding training and conditioning.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### **III. Aeromedical Concerns**

Motion sickness is a common, even normal, physiologic response to an unadapted or unfamiliar movement with significant variation in susceptibility by individuals. The term 'motion sickness' includes airsickness, seasickness, car sickness, space motion sickness, as well as other related entities. It is not typically considered a medical disorder and can be induced in anyone with an intact vestibular system given the right type and duration of provocative stimuli. The effects of motion sickness range from subtle performance deficit and distraction to incapacitation. Motion sickness is thought to occur as a result of conflicting inputs to the brain from visual, vestibular, proprioceptive, and rarely, auditory systems. It is possible to experience characteristic symptoms in the absence of motion, as in the case of "simulator-sickness," "virtual-reality-sickness," or "visually induced motion sickness." The terms 'airsickness' and 'motion sickness' are used interchangeably when seeking waiver.

The USAF has defined two types of airsickness: active and passive. Passive airsickness can include pallor, cold sweats, dizziness, headaches, belching, nausea, apprehension, hyperventilation, lightheadedness, drowsiness and apathy. Active airsickness progresses to retching and vomiting. The affected individual may become distracted even by passive symptoms, leading to a decreased situational awareness and performance degradation. Some individuals may experience significant improvement after vomiting, while others may continue to experience symptoms, including lethargy, fatigue, and drowsiness, long after the motion has stopped. Motion sickness is most commonly encountered among personnel early on in flight training, although it may still occur in more experienced aircrew, especially when switching aircraft types, or when returning to flying after an extended period of non-flying. It is thought that adaption is almost completely retained for 1 month and partially retained for 1 year.

Prevention education and early intervention through the Airsickness Management Program (AMP) have proven to be effective in helping aviator students to overcome motion sickness. The role for pharmacologic intervention is limited in flyers, and may only be utilized early on in pilot training with coordination between the Flight Surgeon and the Aerospace Physiologists per AMP guidelines. Medication usage is not approved for solo flight, or within 5 sorties of solo flight. Approved medications, used as part of the AMP, can be found in the Aircrew Med List on the KX and are not approved for use in trained aviation personnel. Medication use, efficacy, and side effects should be

documented clearly in the medical record and in the AMP reporting tools with the final outcome of each case documented and tracked for annual reporting to AETC/SGP. For more information about the AMP and medication usage, see AETCI 48-102.

It is important to consider the aeromedical and safety concerns related to airsickness, as the effects can range from mild distraction to near-incapacitation. The corresponding degradation of situational awareness and performance is incompatible with flying duties. Most affected aircrew will adapt with repeated exposures to the flying environment, so it is important to keep flying them as often as possible, but in a safe manner (with an IP). Trained aircrew who experience their first episode of airsickness should be evaluated by the flight surgeon to rule out an organic or psychiatric etiology. If no such etiology is found, the affected individual should be enrolled in the AMP at the local base prior to determining a final aeromedical disposition.

AIMWTS search for Motion Sickness waivers within the past 5 years, found 57 total waiver cases with a diagnosis of motion sickness. There were 13 FC I/IA cases (6 disqualified, 54% waived), 10 FC II cases (3 disqualified, 70% waived), 3 RPA pilot cases (100% waived), 30 FC III cases (24 disqualified, 20% waived). To note, the majority of cases not waived were due to other disqualifying diagnoses also in the waiver package, or a DQ recommendation by the local flight surgeon for ARMA-UNSAT. Only a few DQs were truly due to severely debilitating motion sickness unresponsive to therapy.

| ICD-9 code for Motion Sickness |                 |
|--------------------------------|-----------------|
| 994.6                          | Motion sickness |

| ICD-10 code for Motion Sickness |                                    |  |
|---------------------------------|------------------------------------|--|
| T75.3XXA                        | Motion sickness, initial encounter |  |
| T75.3XXD                        | Motion sickness,                   |  |
| T75.3XXS                        | Motion sickness, sequelae          |  |

### **IV. Suggested Readings**

- 1. Parmet AJ and Ercoline WR. Spatial Orientation in Flight. Ch. 6 in *Fundamentals of Aerospace Medicine*, 4<sup>th</sup> ed. Williams and Wilkins, Philadelphia, 2008: 195-203.
- 2. Murdin L, Golding J, and Bronstein A. Managing Motion Sickness. BMJ, 2011; 343: 1213-17.
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- 4. Hu S and Stern RM. The Retention of Adaptation to Motion Sickness Eliciting Stimulation. Aviat Space Environ Med, 1999; 70(8): 766–68.
- 5. Golding JF and Gresty MA. Motion sickness. Curr Opin Neurol, 2005; 18: 29-34.
- 6. Benson AJ, Stott, JRR. Motion Sickness. Ch. 29 in *Ernsting's Aviation Medicine* 5<sup>th</sup> ed. CRC press, 2016 pp. 781-796.
- 7. Official Air Force Aerospace Medicine Approved Medications, 25 Sep 2018.

- 8. AETC Instruction 36-2605, Vol 1, Formal Flying Training Administration and Management, Chapter 3.3, 16 Feb 2016.
- 9. AETC Instruction 48-102, *Medical Management of Undergraduate Flying Training Students*, Chapter 15, 7 Mar 2019.

# **Multiple Sclerosis and Central Demyelinating Disorder (Mar 2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated Table 1 and References

#### I. Waiver Consideration

The diagnosis of multiple sclerosis (MS), clinically or radiographically isolated syndrome (CIS/RIS), or other central demyelinating conditions such as optic neuritis, transverse myelitis, and neuromyelitis optica spectrum disorder, is disqualifying for all flying classes. As the diagnosis of MS is disqualifying for retention purposes, all flying and special operational personnel will require a waiver for this diagnosis. Along with submission of aeromedical waiver request, an initial RILO, or MEB as directed, must be performed to determine military service retention. Members who are retained in military service may then be aeromedically considered. Due to disease unpredictability and effects of military/environmental stressors on symptoms, waiver is generally not recommended for aviators with the diagnosis of MS or high-risk CIS/RIS. However, aviators with CIS/RIS and selected aviators with high-risk CIS/RIS or MS with long-term longitudinal stability may be considered for aeromedical waiver on an individual basis.

Table 1: Waiver potential for multiple sclerosis, CIS/RIS, and other central demyelinating disorders

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------|------------------|--------------------------|
| FC I/IA           | No               | AETC             | No                       |
| FC II//III/SWA    | Yes <sup>1</sup> | AFMRA            | Yes                      |
| ATC/GBO           | Yes <sup>1</sup> | AFMRA            | Yes                      |

<sup>1.</sup> If low-risk CIS/RIS, or longitudinally-stable (clinical and radiographic) high-risk CIS/RIS or MS

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

#### A. Initial Waiver Request:

- 1. A complete discussion of the history of the demyelinating disorder.
- 2. Reports of consultations and diagnostic testing, including: neurology and (as applicable) ophthalmology consultations, reports and images from neuroimaging studies, laboratory testing (including lumbar puncture/cerebrospinal fluid studies, if performed), and sleep study reports (if performed). If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical, mental status and neurologic examination findings.
- 4. Neuropsychological testing if performed. Contact ACS Neuropsychology for questions or further guidance on need for testing and on which tests to administer.
- 5. RILO/MEB results, if obtained.

6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical, neurologic and mental status examination findings.
- 4. RILO/MEB updates as applicable.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual neurologic or cognitive symptoms and signs and any medication effects on operational safety and mission effectiveness, and future risk of symptom development, which could be subtle and unrecognized. Initial imaging and cerebrospinal fluid findings in CIS/RIS cases can stratify for low or high risk of future conversion to MS. Unfortunately, there are no current clinical, biochemical or radiographic markers to prospectively identify those patients who will have 'benign' MS, and assessment of disease stability is based on retrospective analysis only. Even 'benign MS' patients with 10+ years of disease stability have an over 1% annual risk of developing new symptoms between years 10-20. Cognitive deficits are common and unpredictable effecting approximately 40-60% of MS patients. The incidence of cognitive impairments does not correlate well with the degree of physical deficits, as these may be present in all types of MS and at any stage of the disease. Aeromedically-valid neurocognitive testing can be performed only at a maximum of six month intervals. However, even with this level of monitoring, unpredictable interim neurocognitive changes could still pose a threat to self, crew safety, and mission completion. A further concern with MS is the potential of sleep disturbance that can result in daytime sleepiness, worsening fatigue, depression, and lowered pain threshold. Of particular importance, fatigue is considered the most frequent and often the most disabling symptom of MS, reported by at least 75% of patients at some point during their disease course. Finally, none of the current FDA-approved disease-modifying agents are approved for use in aviators due to their side effect profiles.

AIMWTS search in Jan 2019 revealed 100 cases diagnosed as MS, CIS, or as compatible with demyelinating disease. Breakout of the cases was: 3 FC I/IA cases (2 disqualified); 47 FC II cases (36 disqualified); 34 FC III cases (27 disqualified); 5 RPA pilot cases (2 disqualified); 7 ATC/GBC cases (7 disqualified); and 4 MOD cases (1 disqualified). There are several cases of MS not recommended for waiver by ACS, but granted an Exception to Policy from AF/A3 (continuity of ETPs is handled administratively as waivers from AFMRA).

| ICD-9 Codes for MS and CIS |  |  |
|----------------------------|--|--|
| Multiple sclerosis         |  |  |
| 377.30                     | Optic neuritis, unspecified                            |  |
| 341                        | Other demyelinating diseases of central nervous system |  |

| ICD-10 Codes for MS and CIS |  |
|-----------------------------|--|
| G35 Multiple sclerosis      |  |
| H46.9                       | Optic neuritis, unspecified                            |
| G37.8, G37.9                | Other demyelinating diseases of central nervous system |

# IV. Suggested Readings

- 1. Solomon AJ. Diagnosis, differential diagnosis, and misdiagnosis of multiple sclerosis. Continuum (Minneap Minn) 2019; 25(3):611-635.
- 2. Gross RH, Corboy JR. Monitoring, switching, and stopping multiple sclerosis disease-modifying therapies. Continuum (Minneap Minn) 2019; 25(3):715-735.
- 3. Tonin WO. Management of multiple sclerosis symptoms and comorbidities. Continuum (Minneap Minn) 2019; 25(3):753-772.
- 4. Rae-Grant A et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2018; 90:777-788.
- 5. Thompson AJ et al. Diagnosis of multiple sclerosis: 2017 revision of the McDonald criteria. Lancet Neurol 2018; 17:162-173.
- 6. Olek MJ, Howard J. Management of clinically and radiographically isolated syndromes suggestive of multiple sclerosis. UpToDate, Apr 23, 2019.
- 7. Olek MJ, Howard J. Evaluation and diagnosis of multiple sclerosis in adults. UpToDate, Oct 30, 2019.
- 8. Olek MJ, Mowry E. Disease-modifying treatment of relapsing-remitting multiple sclerosis in adults. UpToDate, Jan 2, 2020.
- 9. Novakova L et al. Monitoring disease activity in multiple sclerosis using serum neurofilament light protein. Neurology 2017; 89:2230-2237.
- 10. Sartori A, Abdoli M, and Freedman MS. Can we predict benign multiple sclerosis? Results of a 20-year long-term follow-up study. J Neurol, 2017; 264(5):1068-1075.
- 11. Ropper AH, Samuels MA, Klein JP (Ed). Multiple sclerosis and other inflammatory demyelinating disorders. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:915-945.
- 12. Optic Neuritis Study Group. Multiple Sclerosis Risk After Optic Neuritis: Final Optic Neuritis Treatment Trial Follow-up. Arch Neurol 2008; 65:727-732.
- 13. Rogers JM and Panegyres PK.. Cognitive impairment in multiple sclerosis: Evidence- base analysis and recommendations. J Clin Neuroscience 2007; 14:919-927.

#### WAIVER GUIDE

Updated Jun 2016

Supersedes Waiver Guide of Aug 2012

By: Capt Ashley Franz (RAM 17), Lt Col Eddie Davenport (ACS chief cardiologist) and Dr Dan Van Syoc

### **CONDITION:**

**Myocardial Infarction (Jun 2016)** 

### I. Waiver Considerations.

Myocardial infarction is disqualifying for all classes of flying duty as well as retention. ACS review and evaluation is required, in all cases, for waiver consideration. Waiver is restricted to low performance aircraft (defined as < 2.5 sustained +Gz) and may be considered for all trained aircrew; for pilots, the waiver is additionally restricted to flying with another qualified pilot. Waiver for trained aircrew was approved by the Aerospace Medicine Corporate Board in 2008. Myocardial infarction is also listed specifically as disqualifying for ATC, GBO, and SWA duties.

For aviators, criteria for waiver consideration include, normal left ventricular systolic function at rest and exercise (normal ejection fraction), adequate medical management (lipids, ASA use, HTN control, no diabetes), restricted to low performance aircraft (<2.5 Gz and with another qualified pilot), patent infarct-related artery, no noninvasive testing evidence of reversible ischemia off cardioactive medications at rest and at peak stress, and successful risk factor modification at initial ACS evaluation and at each re-evaluation. If revascularization has been performed, they must meet criteria for the coronary artery revascularization waiver policy. Initial minimum DNIF observation period is six months post-MI. ACS evaluation for initial waiver consideration will include complete noninvasive testing and coronary angiography. If waiver is recommended and granted, waiver will be valid for one year with annual ACS re-evaluation required for waiver renewal consideration. In addition, routine serial coronary angiography is required at five-year intervals. This is based on a review of ACS database of repeat angiography, which shows no recurrent disease at three years following coronary revascularization. This is also consistent with recommendations in the current literature for repeat coronary angiography following revascularization. Follow-up coronary angiography may be recommended sooner if indicated by symptoms, noninvasive test results or failure to control risk factors.

**Table 1: Myocardial infarction and Waiver Potential** 

| Flying Class                                  | Waiver Potential | ACS               |
|---|------------------|-------------------|
|   | Waiver Authority | Review/Evaluation |
| I/IA  | No               | NA                |
| Untrained II and III                          | AETC             |                   |
| II  | No               | NA                |
| IIA (flight surgeon, navigator)* IIC (pilot)* | Yes<br>AFMRA     | Yes, Annual Visit |
| III*  | Yes<br>AFMRA     | Yes, Annual Visit |
| ATC/GBO/SWA                                   | Yes<br>AFMRA     | Review possible** |

<sup>\*</sup> Aircrew must meet all of the following criteria for consideration: normal LVEF, no wall motion abnormality, adequate medical management (including statin, ASA, nitroglycerine (PRN), ACE inhibitor and/or  $\beta$  blocker as clinically appropriate), controlled hypertension, no diabetes or other co-morbidities. Low performance aircraft defined as <2.5 sustained G with another qualified pilot. No altitude restriction in low performance aircraft.

AIMWTS review in May 2016 revealed 76 submitted cases with a history of myocardial infarction. There were 0 FC I cases, 37 FC II cases (21 disqualifications), 32 FCIII cases (23 disqualifications), 6 ATC/GBC cases (2 disqualifications), and 1 MOD case (0 disqualifications).

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations, and the MEB has recommended return to duty.

The AMS for the initial waiver for myocardial infarction should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. Complete history of the event, emergency care rendered, testing done to include all results.
- C. Copy of the cardiac catheterization report and copy of the images (CD, cineangiogram or videotape).
- D. Additional local cardiac testing is not routinely required but may be requested in individual cases.
- E. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. electrocardiogram, treadmill, nuclear myocardial stress perfusion imaging).
- F. Results of MEB returning member to worldwide duty.

<sup>\*\*</sup> Annual testing may be done locally and sent to ACS for review at the request of the MAJCOM, alternatively all testing and follow-up can be done during annual ACS evaluations.

The AMS for <u>waiver renewal</u> for myocardial infarction should include the following: A. Interval history since last waiver – any history of chest discomfort, shortness of breath, or fatigue.

B. Recent ECGs and any other applicable cardiac testing.

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:
Attn: Case Manager for (patient's MAJCOM)
USAFSAM/Aeromedical Consultation Service
2510 5<sup>th</sup> Street, Bldg. 840
WPAFB, OH 45433

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

### III. Overview.

Myocardial infarction (MI) is a common problem in the United States, especially in the general population. Each year, approximately 735,000 Americans have an MI; for 525,000 of these people, it is their first event. Importantly, an estimated 20% of people have "silent" MIs and do not even know that they suffered from an incident.<sup>1</sup>

In the military, and the flying community in particular, MIs are far less common than in the general population. In this population, MI presents as it does in the general population; as an acute, symptomatic event or as a silent event. Such events are often discovered as a result of cardiac testing performed for other indications, such as evaluation of an asymptomatic aircrew with new Q waves on ECG. Post-MI outcomes are similar in these two scenarios and depend primarily on residual left ventricular function, severity of coronary artery disease (CAD), and classic risk factors.<sup>2</sup>

ACS cardiology staff members published a recent study regarding military aviators who have cardiac disease and an MI. This study shows that annual "cardiac event" rates in presumed healthy USAF aviators are 0.15% for males aged 35-54 years. Of particular note, for those aviators who eventually require revascularization, 34% had the MI at initial presentation. Tests designed to screen for MI in the presumed healthy aviator population yield a positive predictive value of 13%. Thus, the screening tests are not good predictors of the risk for MI in the aviator population. Fortunately, the aviators tend to have a much better outcome post CAD diagnosis than does the general population.<sup>3</sup>

There is increasing US Air Force experience with MI in aircrew since a policy change in 2008 allowing waivers for that condition. Policy previously did not allow for a waiver, but an analysis of the Aeromedical Consultation Service (ACS) coronary angiography database provides outcome data in former US Air Force aircrew. Between 1971 and 1999, 1487 asymptomatic male military aviators had an occupational coronary angiogram, and were followed for the cardiac end-points of cardiac death, nonfatal MI and coronary artery revascularization. During the follow-up, 57/1487 aviators (3.8%) had an MI as their first cardiac event. Their MI date was defined as the index date, and post-MI events were calculated at one, two and five year intervals. The events considered

were: cardiac death, non-fatal second MI or first revascularization. No cardiac deaths or second MIs occurred within the 5 years of follow-up; all events were revascularizations. The calculated event rates were 4.0% per year at one year, 2.3% per year at two years and 2.4% per year at five years.<sup>4</sup>

The experience in the medical literature with MI in young populations is very sparse and therefore unreliable. It is also not very generalizable because of high variance in selected groups in term of baseline medical conditions (diabetes, dyslipidemias, HTN) and different degrees of physical fitness. Despite these limitations, the rate of cardiac events is similar to the ACS experience. Batalla published a 2003 follow-up study of 229 male patients younger than 50 years old after their initial MI. The mortality at 3 years was 5% (annual rate of 1.6%) and for a repeat MI at 3 years was 4% (annual rate of 1.3%).<sup>5</sup>

Lopes published a 2008 study reporting on a cohort of 825 patients followed at a large medical center, comparing outcomes in patients with single vessel disease (SVD), two vessel disease (2VD) and three-vessel disease (3VD). All patients had preserved left ventricular ejection fraction (LVEF) and optimal medical therapy (ASA, nitrates,  $\beta$  blockers, ACE inhibitors, statins and low fat/cholesterol diet). The patients with SVD, which are closer to the intended AF population, had a mortality of 1.2% per year and a new MI-rate of 1.3% per year.<sup>6</sup>

In summary, the post-MI event rate in the medical literature is about 2-3% per year in aeromedically appropriate populations. Low risk outcomes are attained by patient selection: absence of premorbid conditions like diabetes, no significant myocardial scars with normal left ventricular systolic function and no significant dysrhythmias following MI, aggressive reduction of risk factors (HTN, lipids, complete smoking cessation, weight control, dietary changes and regular physical activity).

#### IV. Aeromedical Concerns.

The aeromedical concern is recurrent myocardial ischemia presenting as sudden cardiac death, second myocardial infarction, angina or ventricular dysrhythmias, all of which may cause sudden incapacitation or seriously impact performance of flight duties. Detecting the asymptomatic progression of CAD reliably without frequent invasive testing or noninvasive monitoring is the aeromedical challenge.

| ICD-9 Code for myocardial infarction |                             |
|--------------------------------------|-----------------------------|
| 410                                  | Acute myocardial infarction |

| ICD-10 Codes for myocardial infarction |   |
|--|---|
| I21.09                                 | Acute myocardial infarction                 |
| I21.3                                  | ST elevation (STEMI) MI of unspecified site |
| I21.4 Non- ST elevation (STEMI) MI     |   |

#### V. References.

- 1. <a href="http://www.cdc.gov/heartdisease/heart\_attack.htm">http://www.cdc.gov/heartdisease/heart\_attack.htm</a>. Accessed 16Oct15.
- 2. Database, USAFSAM/FEC (Clinical Sciences Division), Wright Patterson Air Force Base, OH.
- 3. Davenport E, Palileo EV, and Gore S. Heroes with Heart Disease: Why United States Air Force Aviators get and Survive Coronary Artery Disease and may Continue to Fly. J Am Coll Cardiol, 2014; 63(12): 61669-7.
- 4. Cole JH, Miller JI, Sperling LS, and Weintraub WS. Long-Term Follow-Up of Coronary Artery Disease Presenting in Young Adults. J Am Coll Cardiol, 2003, 41: 521-28.
- 5. Batalla A, Reguero JR, Martín M, et al. Prognosis of coronary disease in young adults Letter to the Editor. Int J Cardiol, 2004; 97: 327.
- 6. Lopes NH, Paulitsch FS, Gois AF, et al. Impact of number of vessels disease on outcome of patients with stable coronary artery disease: 5-year follow-up of the Medical Angioplasty, and bypass Surgery Study (MASS). Eur J Cardio-Thoracic Surg, 2008; 33: 349-54.
- 7. Fournier JA, Cabezón S, Cayuela A, et al. Long-Term Prognosis of Patients Having Myocardial Infarction When ≤ 40 Years of Age. Am J Cardiol, 2004; 94: 989-92.
- 8. Zimmerman FH, Cameron A, Fisher LD, and Ng G. Myocardial Infarction in Young Adults: Angiographic Characterization, Risk Factors and Prognosis (Coronary Artery Surgery Registry). J Am Coll Cardiol, 1995; 26(3): 648-53.
- 9. Ford ES and Capewell. S. Coronary Heart Disease Mortality Among Young Adults in the U.S. From 1980 Through 2002: Concealed Leveling of Mortality Rates. J Am Coll Cardiol, 2007; 50: 2128-32.
- 10. Anderson RE, Pfeffer MA, Thune JJ, et al. High-risk myocardial infarction in the young: The VALsartan In Acute myocardial iNfarction (VALIANT) trial. Am Heart J, 2008; 155: 706-11.
- 11. Kruyer WB and Davenport ED. Cardiology. Ch. 2 in: *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., Castle Connolly Graduate Medical Publishing, LTD, New York, 2013.
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- 13. Kruyer WB, Delgado A, Myocardial infarction in military aviators and suitability for return to flying. Minutes of the Aerospace Medicine Corporate Board; Oct 8-9, 2008; Hurlburt Field, FL.
- 14. Strader JR, Jr, Gray GW, Kruyer WB. Clinical Aerospace Cardiovascular Medicine. In *Fundamentals of Aerospace Medicine*, 4<sup>th</sup> ed., Lippincott Williams & Wilkins, Philadelphia, 2008. WAIVER GUIDE

*Updated: Feb 2017* 

Supersedes Waiver Guide of Aug 2013

By: Lt Col Cindy Harris Graessle (RAM 17) and Dr. Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

#### **CONDITION:**

Non-Hodgkin's Lymphoma (Feb 2017)

#### I. Waiver Considerations.

History of Non-Hodgkin's lymphoma (NHL) is disqualifying for all flying classes in the US Air Force, as well as for ATC/GBC and MOD personnel, and like all malignancies, will require MEB action.

Table 1: Waiver potential for Non- Hodgkin's Lymphoma

| Flying Class (FC) | Condition  | Waiver Potential ACS |                      |
|-------------------|------------|----------------------|----------------------|
|                   |            | Waiver Authority     | review/evaluation    |
| I/IA              | All stages | Maybe*+              | Maybe†               |
|                   |            | AETC                 |                      |
| II/III            | All stages | Yes*#+               | Yes†                 |
|                   |            | AFMRA                |                      |
| ATC, GBO and SWA  | All stages | Yes*#+               | At the discretion of |
|                   |            | AFMRA                | the waiver authority |

<sup>\*</sup> FC I/IA candidates, as well as untrained FC II, FC III, GBO, SWA, and ATC; waiver may be considered five years after completion of treatment if asymptomatic and in full remission with a favorable prognosis.

AIMWTS review in Nov 2016 revealed a total of 46 cases. Breakdown of the cases was as follows: 5 FC I/IA cases (2 disqualified); 21 FC II cases (6 disqualified); 1 RPA case (0 disqualified); 13 FC III cases (4 disqualified); 4 ATC/GBC cases (0 disqualified); and 2 MOD cases (1 disqualified), for a total of 13 disqualified cases, most which were due to the NHL diagnoses.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>#</sup> For trained FC II, FC III, ATC, GBO, and SWA individuals only, waiver may be considered six months after completion of treatment if asymptomatic and in full remission; the <u>exception</u> is for fighter aircrew who need to wait 12 months prior to waiver consideration if they received bleomycin, otherwise 6 months.

<sup>+</sup> No indefinite waivers will be granted.

<sup>†</sup> For high performance (routine use of aviator mask while flying) individuals treated with bleomycin, <u>will no longer</u> require an ACS evaluation unless problems arise and the evaluation is requested by the waiver authority.

The AMS for initial waiver for NHL should include the following:

A. History – initial symptoms, pathology, stage, treatment, surveillance plan, and activity level. History should also emphasize past personal or family history of malignancy, radiotherapy, chemotherapy, connective tissue disease, or immune-suppression.

- B. Physical exam.
- C. Hematology/oncology reports to include all follow-up studies consistent with current guidelines in National Cancer Comprehensive Network (NCCN).<sup>6</sup>
- D. Lab/Rad –CBC, peripheral smear, serum creatinine, Complete metabolic panel, hepatitis panel and HIV serology. Serum beta-2 microglobulin levels for individuals with indolent NHL and serum protein electrophoresis for individuals with small lymphocytic lymphoma. Submit bone marrow and CSF studies if clinically indicated and obtained. Chest x-ray and any other imaging studies to include CT, endoscopic photographs, and PET scans should be provided. Submit echocardiogram or MUGA scan studies if the individual is treated with anthracycline containing regimens. Submit completed pulmonary function studies (any additional PFTs will be done in conjunction with the ACS evaluation).
- E. Tumor board report, military or civilian, if applicable.
- F. Medical evaluation board results (MEB).

The AMS of <u>waiver renewal</u> of NHL should include the following:

- A. History brief summary of stage, treatment, frequency of surveillance with results, symptoms, and activity level.
- B. Physical exam.
- C. Hematology/oncology consultation reports.
- D. Lab/Rad CBC, peripheral smear, complete metabolic panel, beta-2 microglobulin, and serum protein electrophoresis as clinically indicated.
- E. All treatments and follow-up consistent with current guidelines in the NCCN.<sup>6</sup>
- F. Any RILO summaries associated with persistent Assignment Limitation Codes.

# III. Overview.

NHL is a diverse group of lymphoid malignancies and can range from aggressive to more indolent in behavior. More recent classifications have taken into account genetic information as well as cell morphology to better characterize the behavior of these neoplasms in individual patients. Additionally, it is also recognized that there is a continuum between leukemias and lymphomas and that they can represent the same disease entity. There is an estimated 1 in 47 lifetime risk of being diagnosed with NHL, with approximately 75% of cases diagnosed at age 75 or older. While the incidence of the disease has been increasing, so has the efficacy of the therapies, imparting a 5 year survival rate of 68.1%.

Abnormal immunologic status, certain viruses and bacteria, occupational exposures, and history of prior lymphoma have all been attributed to an increased risk of NHL. Presentation can include fever, weight loss, and sweats (B symptoms). Often, a patient will be asymptomatic except for an enlarging lymphatic mass.

The physical examination of individuals with suspected NHL should be directed at all lymphoid tissue sites and include special attention to the liver and spleen. Initial laboratory evaluation should include CBC, peripheral smear, complete metabolic panel, protein electrophoresis, hepatitis, and

HIV serology. Beta-2 microglobulin and bone marrow aspirate and biopsy should be obtained if indicated. Cerebrospinal Fluid (CSF) studies may also be indicated in the evaluation of CNS NHL. Biopsy tissue confirmation is essential for definitive diagnosis and therapy.

Initial imaging should include chest x-ray and computed tomography of the chest, abdomen, and pelvis. MRI of the brain is indicated for evaluation of CNS NHL. Positron emission tomography (PET) scanning may be helpful in determining the location of NHL and for monitoring treatment response.

The Ann Arbor Staging System with the Cotswold modifications is the standard for staging of NHL. Treatment is driven not only by staging, but also by molecular genetic factors and individual response to therapy.<sup>3</sup>

Table 2: Cotswold Modification of Ann Arbor Staging System<sup>4</sup>

| Stage                       | Area of Involvement  |  |
|-----------------------------|--|--|
| I                           | Single lymph node group  |  |
| II                          | Multiple lymph node groups on same side of diaphragm               |  |
| III                         | Multiple lymph node groups on both sides of diaphragm              |  |
| IV                          | Multiple extranodal sites or lymph nodes and extranodal disease    |  |
| X                           | Bulk > 10cm  |  |
| E                           | Extranodal extension or single isolated site of extranodal disease |  |
| A (not present)/B (present) | B symptoms: weight loss > 10%, fever, drenching night sweats       |  |

Treatment principles take into account the heterogeneous nature of NHL, cell cycle control, drug resistance, and dose intensity. Treatment regimens vary widely from radiation only for indolent early stage disease to aggressive multi-drug regimens with bone marrow transplant for more aggressive NHL. A common feature of current treatment regimens is the use of rituximab. Rituximab is an anti-human CD20 monoclonal antibody that increases the efficacy of other chemotherapeutic regimens but can also be used as monotherapy. Newer therapies have changed the prognosis of NHL and future prognostic indices will likely be highly individualized. The most up to date treatment guidelines are detailed in the National Cancer Comprehensive Network Clinical Practice Guidelines in Oncology (NCCN).

### IV. Aeromedical Concerns.

As with most malignancies, aeromedical concerns of NHL are based on the disease as well as the treatment regimen. With NHL, the risk for sudden incapacitation is minimal as disease involvement of the CNS or heart is rare. Although the most common presentation of NHL is peripheral lymphadenopathy, initial manifestations rarely may include neurologic symptoms from central nervous system involvement or spinal cord compression.

NHL survivors who received chemotherapy have the potential to suffer adverse consequences in relation to their work life and have poor perceptions of their health compared to peers as long as 5 to 15 years after completion of therapy. They can also suffer from excess fatigue as long as 10 years after diagnosis. The source of this fatigue is multi-factorial and cannot be attributed solely to mode of treatment. Although treatment regimens can be potentially neurotoxic, there is some

evidence that the long term neuropsychiatric sequelae are minimal. NHL survivors are at higher risk for second malignancies. This increased risk is likely related to therapy, but genetic predisposition and environmental exposures may also be involved. NCCN follow-up guidelines take into account this increased risk.

In the past, the use of bleomycin in aviators would have been permanently disqualifying. This was based on the risk of pulmonary fibrosis with exposure to oxygen. The value of bleomycin in the treatment of malignancies is in part a function of its specific toxicity, since it does not induce bone marrow aplasia, and thus does not add to the toxicity that limits most oncologic drugs. Instead, the principal target organ of bleomycin-induced injury is the lung, with acute pulmonary damage occurring in 6-18% of treated patients. The pathophysiology of delayed toxicity of bleomycin is complex. In the medical literature of the last thirty years, a number of patients have been described who, having previously received bleomycin therapy; have developed pulmonary toxicity when undergoing subsequent surgery. Typically, these have been young individuals receiving modest levels of oxygen (33-42%) during long operations (4-8 hours). The true incidence of such delayed toxicity is unknown, since the subsequent literature has largely consisted of isolated case reports or small series. A more cogent argument can be made that the period of risk is primarily in the first year after therapy, since most cases occurred within that time frame. However, it is equally possible that this observation represents a bias related to the timing of operative intervention.

Applicable data had been non-existent, a state of affairs that has been somewhat altered by unpublished data recently supplied by the Duke Hyperbaric Unit.<sup>11</sup> Although it had been the practice in hyperbaric medicine to avoid hyperoxia in bleomycin-treated individuals, the undoubted benefit from hyperbaric oxygen (HBO) in wound healing and osteonecrosis posed against the uncertain risk of delayed bleomycin toxicity led several years ago to a change in policy. Since then, the Duke unit has treated 11 individuals previously exposed to bleomycin with HBO. There was a wide range of time between the last dose of bleomycin and the institution of HBO, ranging from 1 month to 22 years. The range of cumulative bleomycin doses was not noted. Anywhere from 8 to 44 treatments with 100% oxygen at 2 ATA (PiO2 ~ 1475 mmHg) were administered for two hours per treatment, once or twice daily. One individual experienced significant chest discomfort and a decline in diffusion capacity of 50%; both resolved following a break in treatment, and she successfully completed HBO treatment with a reduction in frequency of her sessions. While the Duke experience does not represent occupational exposure per se, and the number of individuals treated is small, the amount of oxygen exposure from HBO therapy is far in excess of what would be expected in aviation, suggesting that the risk of delayed toxicity outside the operating room may be minimal<sup>12, 13</sup>.

Based on this data, policy was changed for aviators treated with bleomycin. Those aviators returning to non-high performance aircraft would be evaluated as usual, addressing risks of tumor recurrence and potential toxicity from chemotherapy. Assuming they had not developed bleomycin pneumonitis during therapy, then no restrictions from altitude chamber or other sporadic oxygen exposure is warranted. Because it is possible, and biologically plausible, that the common perception of an increased period of risk within the first year is correct, a grounding period of one year from the end of treatment is required before waiver consideration in high performance aircrew. In most cases, this will coincide with the grounding period already recommended as a result of the disease/chemotherapeutic regimen.

There have been case reports of life-threatening pneumonitis developing in patients with a history of bleomycin-induced lung injury, who were later given supplemental oxygen for surgical procedures. Therefore, aviators who have a history of bleomycin-induced lung injury should not be allowed to return to airframes that require routine use of 100% oxygen. Also, they should be recommended for medical exemption from the portions of the altitude chamber qualification that require 100% oxygen use (in coordination with AOP, A3 and training) from the portions of the altitude chamber qualification that require 100% oxygen use. Use of 100% oxygen during emergencies such as fire or rapid decompression is acceptable and should not be discouraged.

Aviators treated with anthracyclines (e.g. Adriamycin) are at risk of treatment induced cardiomyopathy. The aeromedical risk due to poor left ventricular function as a result of anthracycline-containing treatment regimens requires demonstration of adequate cardiac function. An echocardiogram or Multi-Gated Acquisition (MUGA) scan may be required to demonstrate adequate cardiac function for consideration of returning an aviator to flying following treatment with anthracyclines.<sup>6</sup>

| ICD-9 Code  | Type of Non-Hodgkin's Lymphoma                          |  |
|-------------|---|--|
| 202.8       | Lymphoma (malignant)                                    |  |
| 204.9       | Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma |  |
|             | (CSLL-1)  |  |
| 202.0       | Follicular Lymphoma                                     |  |
| 200.3       | Gastric MALT Lymphoma (MALT-1)                          |  |
| 200.3       | Non-gastric MALT Lymphoma (NGMLT-1)                     |  |
| 200.3       | Nodal Marginal Zone Lymphoma (NODE-1)                   |  |
| 200.3       | Splenic Marginal Zone Lymphoma (SPLN-1)                 |  |
| 200.4       | Mantle Cell Lymphoma (MANT-1)                           |  |
| 200.7       | Diffuse Large B-Cell Lymphoma (BCEL-1)                  |  |
| 200.2       | Burkitt's Lymphoma (BURK-1)                             |  |
| 200.1       | Lymphoblastic Lymphoma (BLAST-1)                        |  |
| 202.7       | Peripheral T-Cell Lymphoma (TCEL-1)                     |  |
| 202.1/202.2 | Mycosis Fungoides/Sezary Syndrome (MFSS-1)              |  |
| 200.5       | Primary CNS Lymphoma                                    |  |

| ICD-10 Code | Type of Non-Hodgkin's Lymphoma                                  |  |
|-------------|---|--|
| C85.80      | Other specified types of non-Hodgkin lymphoma, unspecified site |  |
| C91.90      | Lymphoid leukemia, unspecified not having achieved remission    |  |
| C82.80      | Other types of follicular lymphoma, unspecified site            |  |
| C83.80      | Other non-follicular lymphoma, unspecified                      |  |
| C83.87      | Other non-follicular lymphoma, spleen                           |  |
| C83.88      | Other non-follicular lymphoma, lymph nodes of multiple sites    |  |
| C88.4       | Extranodal marginal zone B-cell lymphoma of mucosa-associated   |  |
|             | lymphoid tissue (MALT-lymphoma)                                 |  |
| C83.10      | Mantle Cell Lymphoma, unspecified site                          |  |
| C83.39      | Diffuse large B-cell lymphoma, extranodal & solid organ sites   |  |
| C83.38      | Diffuse large B-cell lymphoma, lymph nodes of multiple sites    |  |
| C83.70      | Burkitt's lymphoma, unspecified site                            |  |
| C83.50      | Lymphoblastic (diffuse) lymphoma, unspecified site              |  |
| C84.40      | Peripheral T-cell lymphoma, not classified, unspecified site    |  |
| C84.00      | Mycosis fungoides, unspecified site                             |  |
| C84.10      | Sezary disease, unspecified site                                |  |

#### V. References.

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- 9. Tucker J, Prior PF, Green CR, et al. Minimal neuropsychological sequelae following prophylactic treatment of the central nervous system in adult leukaemia and lymphoma. Br J Cancer, 1989; 60(5): 775-80.
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- 12. Torp KD, Carraway MS, Ott MC, et al. Safe administration of hyperbaric oxygen after bleomycin: A case series of 15 patients. Undersea Hyperbaric Med, 2012; 39(5): 873-79.
- 13. Aakre BM, Efem RI, Wilson GA, et al. Postoperative Acute Respiratory Distress Syndrome in Patients With Previous Exposure to Bleomycin. Mayo Clin Proc, 2014; 89(2) 181-89.

# Ocular Histoplasmosis Syndrome (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator) and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Version. MSD C44.

#### I. Waiver Consideration

Patients who have active OHS lesions are disqualified for all flying class duties. In these cases, waivers will not be considered until the disease has resolved or the active lesions have been adequately treated. If an active lesion is treated by laser photocoagulation or PDT, patients should have at least one follow-up evaluation completed by the treating ophthalmologist 3-4 weeks post therapy prior to waiver submission. Follow-up examination must indicate extent of choroidal neovascularization (CNV) eradication and if residual disease is present requiring further therapy. Inactive lesions which allow the airman to meet vision standards will be waived on a case by case basis. Local ophthalmology evaluation to include visual acuity, Amsler grid testing, Humphrey 10-2 visual fields, stereopsis and funduscopic evaluation are required. Submit any ophthalmologic imaging obtained including optical coherence tomography (OCT) and fluorescein angiography. All cases will need to be reviewed or seen by ACS Ophthalmology. In addition, any disease, injury, infection process, or sequelae involving the eye that is resistant to treatment and/or results in: distant visual acuity that cannot be corrected to the retention vision standards listed in Item C2, and/or a central field of vision defect in the better eye that reduces the field of view less than 20 degrees from fixation in any direction is disqualifying for retention and will require an MEB.

Table 1: Waiver potential for Ocular Histoplasmosis Syndrome

| Flying Class (FC)  | Waiver                     | Waiver                 | ACS Review/Evaluation |
|--------------------|----------------------------|------------------------|-----------------------|
|                    | Potential <sup>1,2,3</sup> | Authority <sup>4</sup> |                       |
| I/IA               | Yes                        | AETC                   | Yes                   |
| II/III (untrained) |                            |                        |                       |
| II/III             | Yes                        | MAJCOM                 | Yes <sup>5</sup>      |
| SWA                |                            |                        |                       |
| ATC/GBO/OSF        | N/A                        | N/A                    | N/A                   |

- 1. History of macular disease or CNV in an initial applicant will not be waived.
- 2. Must meet retention and Flying Class-specific vision standards. Must not be expected to progress or recur. No active or reactivated disease are waiverable.
- 3. No indefinite waivers.
- 4. If individual does not meet retention standard outlined in MSD, then waiver authority becomes AFMRA.
- 5. For initial waiver consideration, AMS goes to AFMRA and subsequent requests may go to MAJCOM.

#### II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### A. Initial Waiver Request:

- 1. List and fully discuss all clinical diagnoses and diagnoses requiring a waiver.
- 2. Eye exam to include:
  - a. Visual acuity
  - b. Humphrey visual fields (30-2 and 10-2)
  - c. Stereopsis testing.
- 3. Ophthalmology consultation report to include all follow-up reports.
- 4. If active lesions are part of the history and were treated by laser photocoagulation, intravitreal injections, or PDT, patients should have at least one follow-up evaluation, at least 3-4 weeks post therapy, completed by the treating ophthalmologist prior to waiver submission.
- 5. Ophthalmologic imaging test results to include fundus photos, OCT, and fluorescein angiography.
  - 6. MEB results, if required.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

# B. Renewal Waiver Request:

- 1. Interim History since last waiver and ACS visit.
- 2. Ongoing treatment modalities.
- 3. Full ophthalmology exam to include Amsler grid, dilated fundus exam, and OCT of the maculae.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

#### **III. Aeromedical Concerns**

The primary aeromedical concern in OHS is its potential to affect central and peripheral vision. Patients with peripheral inactive disease without evidence of macular involvement will maintain excellent visual acuity and have a good visual prognosis. Some of these patients may have residual visual field defects, but most are minor and do not have substantial effects on peripheral vision. For those patients who develop macular disease, the prognosis is more guarded. Progression of disease with loss of vision depends upon the size and location of the lesion, development of CNV, and subsequent scaring. After three years, more than 75% of patients with subfoveal CNV will have a best-corrected visual acuity of 20/100. If the patient is less than 30 years of age and has a small subfoveal CNV lesion with no visual loss secondary to OHS in the other eye, a visual acuity of 20/40 or better may be retained in up to 14% of eyes. Currently, available treatments may preserve vision, although treating the macular area with laser therapy may degrade visual acuity. If subfoveal or juxtafoveal lesions are present, treatment should involve intravitreal anti-VEGF injections, PDT, or a combination of these two.

Review of AIMWTS in Jan 2019 identified 29 cases of OHS submitted for waivers. Of the 29 waivers, 3 were for FCI (1 disqualified), 18 were for FCII (3 disqualified), 2 were for RPA pilots, and 6 were for FCIII (1 disqualified). The waivers returned as medically acceptable all had inactive disease and met vision standards.

| ICD-9 codes for Ocular Histoplasmosis |   |  |
|---------------------------------------|---|--|
| 115.02 Ocular histoplasmosis syndrome |   |  |
| 115.9                                 | Histoplasmosis unspecified without manifestation    |  |
| 115.92                                | 15.92 Histoplasmosis retinitis, unspecified         |  |
| 115.99                                | Histoplasmosis unspecified with other manifestation |  |

| ICD-10 codes for Ocular Histoplasmosis      |  |  |
|---|--|--|
| B39.4 Histoplasmosis capsulati, unspecified |  |  |
| B39.9                                       | 9 Histoplasmosis, unspecified                  |  |
| H32   | Chorioretinal disorders in diseases classified |  |
| elsewhere                                   |  |  |

# IV. Suggested Readings

Moorthy RS. Histoplasmosis. Ch. 7.10 in Yanoff & Duker: Ophthalmology, 3rd ed., Mosby, 2008.

# Optic Nerve Head Drusen (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, Aerospace Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator) and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** New Ground Based Operator (GBO) standards. C54.

### I. Waiver Consideration

Optic nerve head drusen is a disqualifying condition for flying classes I/IA, II, III, and SWA personnel. It is not listed as a disqualifying diagnosis for ATC, GBO (RPA Pilot, RPA SO, and MOD), or OSF personnel, but for ATC/GBO personnel, it would be disqualifying if it results in a visual field defect. Aeromedical Consultation Service (ACS) evaluation is required for initial waiver of optic nerve head drusen for cases eligible for waiver. FC I/IA candidates with optic nerve head drusen are not eligible for waiver. Optic nerve head drusen in untrained FC II and FC III are also typically not eligible for waiver. ACS review is required for waiver renewal; depending on the results of local work-up, an ACS evaluation may be required. Waiver potential is based upon ophthalmologic examination including visual acuity, color vision, stereopsis, absence of transient visual loss, and an absence of aeromedically significant visual field defect.

Table 1: Waiver potential for Optic Nerve Head Drusen.

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review/Evaluation |
|-------------------|------------------|------------------|-----------------------|
| I/IA              | No               | AETC             | No <sup>1</sup>       |
| II/III/SWA        | Yes <sup>2</sup> | MAJCOM           | Yes                   |
| ATC/GBO           | N/A <sup>3</sup> | N/A              | N/A                   |
| OSF               | N/A              | N/A              | N/A                   |

- 1. ACS evaluation only required if diagnosis is in question.
- 2. Waiver for untrained flying class II and III is unlikely but will be considered on a case-by-case basis.
- 3. Waiver will be required if the condition causes loss of visual acuity, visual field, or color vision.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# A. <u>Initial/Renewal Waiver Request:</u>

- 1. Complete aeromedical history to include pertinent positives and negatives (e.g. headaches, pulsatile tinnitus, hypertension, diabetes, family history of drusen, etc.)
- 2. Presence or absence of visual symptoms and their operational impact (e.g. transient visual obscurations, perceived scotomas or metamorphopsia)

- 3. Results of complete optometric or ophthalmologic eye examinations to include:
  - a. Refraction to best Snellen visual acuity
  - b. Intraocular pressure by applanation tonometry
  - c. CCT results for each eye individually
  - d. Amsler grid
  - e. Humphrey visual field testing (preferably 30-2)
  - f. Ocular coherence tomography (OCT) of the retinal nerve fiber layer (RNFL)
  - g. Stereoscopic optic disc evaluation.
- 4. Diagnostic test(s) supporting diagnosis (e.g. ophthalmic B-scan ultrasound, computed tomography of the orbit, or autofluorescence.)
- a. Confirmatory diagnostic testing is only required for the initial diagnosis. Images and report of at least one confirmatory test must be included in the initial waiver request.
- b. Waiver renewal requires items #1 through #3 be performed. The results of the testing in item #4 used for the initial waiver should be included in the AMS with the date and results of the initial testing performed. Confirmatory diagnostic testing is not required for each waiver renewal.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Clinically and aeromedically, the main concern with optic disc drusen is their propensity to induce slowly progressive visual fields loss. As high as 87% of individuals with optic nerve head drusen can expect to have visual field abnormalities. Furthermore, transient disturbances in central acuity and visual field may occur in association with optic nerve head drusen. Color vision anomalies have also been described in 41% of USAF aviators with ODD in preliminary data collected at the Aeromedical Consultation Service. ODD have also been associated with retinal hemorrhage in 2-10% of patients, though most cases are incidental findings without visual impairment.<sup>1</sup>

Once the diagnosis of drusen is established, careful evaluation of optic nerve function is imperative. This should include visual acuity, visual field testing, Amsler grid, and color vision testing. Visual field loss has the most potential for aeromedical grounding and as such, visual field testing should be performed on a regular basis to ensure visual function remains adequate and consistent with mission effectiveness and flying safety. In addition, applanation tonometry should be completed in cases with known visual field or RNFL and GCC loss on OCT. This recommendation comes due to the risk of hypoxic nerve injury. Ischemia is the cause of the visual field loss and optic nerve damage associated with optic nerve head drusen. In a normal healthy optic nerve, the redundancy of blood supply allows aircrew to have adequate blood flow to the optic nerve in most instances, to withstand the hypoxia associated with flight. The optic nerve of a member with drusen is already a compromised nerve. As reported above, even in the civilian population, 71-87%, have ischemic related optic nerve injury even without the hypoxia risk. Optic disc photodocumentation should be obtained for comparison during future monitoring. It is also important for patients to self-monitor their vision periodically with Amsler Grid testing. Periodic surveillance to assess visual function in aircrew with optic nerve head drusen is appropriate, since drusen-related optic nerve problems are often asymptomatic. Routine cases should be monitored every six to twelve months.

AIMWTS search revealed a total of 140 members with an AMS containing the diagnosis of optic nerve head drusen. There were 51 disqualifications in that total. Breakdown of the cases revealed:

24 FC I/IA cases [22 disqualified (2 FC I/IA waivers exist in AIMWITS; both cases were misdiagnosed at the time of waiver submission as optic nerve head drusen and the diagnosis remained. However, subsequently no disc drusen were definitively identified following full ophthalmology evaluation in these individuals)], 54 FC II cases (1 disqualified), 58 FC III cases (26 disqualified), 4 ATC/GBC cases (2 disqualified), and no MOD cases.

| ICD-10 Codes for Optic Nerve Head Drusen |         |                                       |
|--|---------|---------------------------------------|
|  | H47.329 | Drusen of optic disc, unspecified eye |

# **IV. Suggested Readings**

1. Auw-Haedrich C, Staubach F, Witschel H. Optic Disk Drusen. Survey of Ophthalmology, 2002; 47(6): 515-532

# Optic Neuritis (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Version. MSD C49.

### I. Waiver Consideration

Optic neuritis (ON) is disqualifying for flying classes I/IA, II, III, and SWA duties. It is not specifically listed as disqualifying for GBO, ATC, and OSF duties, unless MS has also been diagnosed, in which case the member is disqualified. If the ON is visually symptomatic (decreased visual acuity or visual field defect), it would then be disqualifying for ATC, GBO, and OSF duties.

**Table 1: Waiver potential for Optic Neuritis.** 

| Flying Class (FC)         | Waiver Potential | Waiver Authority    | ACS Review or Evaluation |
|---------------------------|------------------|---------------------|--------------------------|
| I/IA                      | No               | AETC                | No                       |
| II/III/SWA <sup>1,2</sup> | Yes              | MAJCOM <sup>3</sup> | Yes                      |
| ATC/GBO/OSF <sup>2</sup>  | Yes              | MAJCOM <sup>3</sup> | Maybe                    |

<sup>1.</sup> In untrained FC II and III, waiver recommendation is unlikely.

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

#### A. Initial Waiver Request:

- 1. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- 2. A complete discussion of the history of the optic neuritis.
- 3. Results of consultation from Ophthalmology AND Neurology
- 4. Visual Field (30-2) results at initial diagnosis and 3 months later.
- 5. Labs: If lumbar puncture clinically indicated by a neurologist, submit cerebrospinal fluid results including oligoclonal bands and myelin-basic protein.
- 6. Brain T1 and T2-weighted MRI with gadolinium and FLAIR sequences at initial presentation and 3 months later. Send report(s) and images to the ACS. Images may be mailed to ACS on CD or uploaded to the USAFSAM ECG Library PICOM servers.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

<sup>2.</sup> All waivers are recommended to be valid for only one year. ACS evaluations should be "in person" for initial waiver after a normal MRI and a normal repeated MRI 3 months later. Waiver renewal may be performed by review or evaluation.

<sup>3.</sup> If the case also demonstrates positive MRI/CSF or definitive Multiple Sclerosis, the waiver authority is AFMRA.

# B. Renewal Waiver Request:

- 1 Interval history.
- 2 Interval labs (if indicated).
- 3 Interval brain T1 and T2-weighted MRI with gadolinium and FLAIR sequences. Send report(s) and images to ACS. Images may be mailed to ACS on CD or uploaded to the USAFSAM ECG Library PICOM servers.
- 4 Optical Coherence Tomography (OCT) of the retinal nerve fiber layer (RNFL).
- 5 Interval Threshold 30-2 Visual Field Studies.
- 6 Follow-up consultations from Ophthalmology and Neurology.
- 7 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

The primary aeromedical concerns with isolated ON (as defined by the absence of radiologic or clinical criteria for MS) are variable decreases in visual performance that are unpredictable by either clinical exam or imaging study and may go unrecognized by aircrew member with or without treatment. These visual changes include decreased visual acuity, degradation in color vision, visual field defects, and photopsias. Symptoms can present over a period of hours and may increase under physiologic stresses such as dehydration, hypoxia, fatigue, or increases in body temperature. Additionally, Uhthoff's phenomenon, which is a decrease in vision associated with a rise in body temperature, was a common observation amongst USAF aircrew with ON. Military operational extremes characterized by increased heat exposure, such as in desert operations and in hot closed cockpits/crew stations, may place military personnel at an increased risk for Uhthoff related functional impairments.

The risk of relapse from typical isolated ON with normal brain CSF and MRI findings is low enough, as evidenced by the Optic Neuritis Treatment Trial (ONTT), that disease modifying immunomodulatory treatment is not recommended, and waiver is possible. Treatment with high dose intravenous methylprednisolone may be considered to hasten visual return in severe cases with possible earlier return to duty with isolated ON. However, this must be balanced with the risks of such therapy since long term visual performance is not changed. When ON is not isolated, the risk of relapse is very high. Unfortunately, the reduction in relapses seen with treatment is insufficient for aviation purposes and immunomodulatory therapy for MS is not currently approved for waiver. Thus, the issue of treatment is largely irrelevant for aeromedical purposes at this time.

AIMWTS search in Jan 19 revealed 41 cases with the diagnosis of ON. There were 0 FC I/IA cases, 16 FC II cases (8 disqualifications), 22 FC III cases (9 disqualifications), 2 RPA pilot cases (1 disqualification), and 1 ATC/GBC case.

| ICD 9 code for Optic Neuritis |                             |  |
|-------------------------------|-----------------------------|--|
| 377.30                        | Optic neuritis, unspecified |  |

| ICD 10 code for Optic Neuritis |                             |
|--------------------------------|-----------------------------|
| H46.9                          | Optic neuritis, unspecified |
| H46                            | Optic neuritis              |

# **IV. Suggested Readings**

- 1. Clark D, Kebede W, and Eggenberger E. Optic Neuritis. Neurol Clin, 2010; 28: 573-80.
- 2. Optic Neuritis Study Group. The Clinical Profile of Optic Neuritis: Experience of the Optic Neuritis Treatment Trial. Arch Ophthalmol, 1991; 109(12): 1673-78.
- 3. Gerling J, Meyer JH, Kommerell G. Visual field defects in optic neuritis and anterior ischemic optic neuropathy: distinctive features. Graefes Arch Clin Exper Ophthalmol, 1998; 236: 188-92.
- 4. Keltner JL, Johnson CA, Cello KE, et al. Visual Field Profile of Optic Neuritis: A Final Follow-up Report From the Optic Neuritis Treatment Trial From Baseline Through 15 Years. Arch Ophthal, 2010; 128: 330-37.
- 5. Ivan DJ, Tredici TJ, Burroughs JR, et al. Primary Idiopathic Optic Neuritis in U.S. Air Force Aviators. Aviat Space Environ Med, 1998; 69(2): 158-65.
- 6. The Optic Neuritis Study Group. Visual Function More Than 10 Years After Optic Neuritis: Experience of the Optic Neuritis Treatment Trial. Am J Ophthalmol, 2004; 137: 77-83.

#### WAIVER GUIDE

Updated: Apr 2016

Supersedes Waiver Guide of Jan 2013

By: Maj Andrew Timboe (RAM 17) and Dr Dan Van Syoc

Reviewed by: Col Matthew Carroll, AF/SG consultant for Rheumatology

#### **CONDITION:**

Osteoarthritis (Apr 2016)

# I. Waiver Consideration.

Arthritis of any type of more than minimal degree, which interferes with the ability to follow a physically active lifestyle, or may reasonably be expected to preclude the satisfactory performance of flying duties is disqualifying for all classes of flying. If the pain can be controlled with acetaminophen or an aeromedically approved nonsteroidal, the aviator can remain on these medications and be considered for a waiver. A waiver request that includes the use of an NSAID should include, at a minimum, a CBC and a comprehensive metabolic profile to monitor for adverse effects of the treatment, and done so in conjunction with manufacturer's recommendations.

Aviators with significant pain or limitations will need to be grounded until these issues are satisfactorily addressed. If pain and/or limitations persist despite maximal medical therapy, then disqualification from flying duties may need to be considered. If joint replacement is deemed appropriate, then the information in the Retained Orthopedic Hardware and Joint Replacement waiver guide should be followed, for guidance. OA of the spine that requires medical therapy and close observation is not waiverable for ejection seat aircraft. ATC and GBO personnel are covered under retention standards; internal derangement of the knee complicated by arthritis and severe osteoarthritis are listed as disqualifying for retention standards. Any joint pain that interferes with the ability to successfully complete the mission is disqualifying.

**Table 1: Waiver potential for Osteoarthritis** 

| Flying Class | Condition/Treatment      | Waiver Potential  |  |
|--------------|--------------------------|-------------------|--|
|              |                          | Waiver Authority† |  |
| I/IA         | Stable OA on no meds+    | Maybe             |  |
|              |                          | AETC              |  |
|              | Symptoms controlled with | No                |  |
|              | meds                     | AETC              |  |
|              | Symptoms not controlled  | No                |  |
|              | with meds                | AETC              |  |
| II/III       | Stable OA on no meds+    | Yes               |  |
| SWA          |                          | MAJCOM            |  |
|              |                          |                   |  |
|              | Symptoms controlled with | Yes               |  |
|              | meds#+                   | MAJCOM            |  |
|              | Symptoms not controlled  | Maybe             |  |
|              | with meds*+              | MAJCOM            |  |
| ATC/GBO      | Stable OA on no meds+    | Yes               |  |
|              |                          | MAJCOM            |  |
|              | Symptoms controlled with | Yes               |  |
|              | meds#+                   | MAJCOM            |  |
|              | Symptoms not controlled  | Maybe             |  |
|              | with meds*+              | MAJCOM            |  |

<sup>\*</sup>Symptomatic patients who go on to joint replacement may be eligible for a waiver – see Retained Hardware and Joint Replacement Waiver Guide.

Review of AIMWTS data in Mar 2016 revealed 213 cases with the diagnosis of osteoarthritis. Breakdown of the cases revealed: 2 FC I/IA cases (both disqualified); 103 FC II cases (14 disqualified); 96 FC III cases (29 disqualified); 9 ATC/GBC cases (2 disqualified); and 3 MOD cases (none disqualified). Of the 47 disqualified cases, 17 cases were disqualified due to severe joint disease and 30 cases for multiple medical problems which included varying degrees of joint disease.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>#</sup>Medications used to control OA must be on the approved medication list; see note at end of Aeromedical Concerns for appropriate f/u if on chronic NSAIDs.

<sup>+</sup>No indefinite waivers; waiver should be renewed approximately every three years if stable.

<sup>†</sup>If member does not meet retention standards, then the waiver authority is AFMRA.

The AMS for <u>initial waiver</u> for osteoarthritis should include the following:

- A. History of symptoms, history of trauma and activities, limitations secondary to disease, summary of all treatments to date, present level of activity, medications (including over the counter medications), and functional limitations. Document gastrointestinal and/or renal symptoms and signs related to medications taken, if present.
- B. Physical addressing range of motion, tenderness, edema/effusion, deformity, associated muscle strength/atrophy and neurologic signs (if symptoms/ present). Document skin/nail findings, if abnormal.
- C. Labs: ESR as clinically indicated. RF is not needed unless there are clinical indications to do so. CBC and metabolic profile if on NSAIDs for three or months continually; at three months and then periodically if WNL. Synovial fluid analysis, if clinically indicated.
- D. Orthopedic or rheumatology consultation report (general internal medicine will suffice if orthopedics and rheumatology not available). Physical therapy evaluation for range of motion, muscle strength, activity level, and limitations.
- E. Operative reports, if applicable.
- F. Results of X-rays; X-rays should always be ordered based on clinical findings with results interpreted in the context of the patient's symptoms and the American College of Rheumatology (ACR) classification criteria. MRI and X-Rays have significant discord with clinical findings. In general, MRI detects more asymptomatic degenerative changes and X-Rays can miss some degenerative symptomatic findings. Additionally, sometimes OA progresses radiographically with little clinical change. When available, radiographic studies can be helpful, but they are not a reliable diagnostic or monitoring tool. ACR classification criteria allow you to diagnose knee OA without radiographs.
- G. Medical evaluation board (MEB) results (if applicable).

The AMS for <u>waiver renewal</u> for osteoarthritis should include the following:

- A. Interim history and physical focus on any changes since most recent waiver, present level of activity, medications, and limitations.
- B. Applicable consult(s).
- C. X-rays and lab results, if applicable.
- D. RILO (if applicable)

### III. Overview.

Osteoarthritis (OA) is the most common joint disease worldwide, affecting an estimated 27 million Americans alone.<sup>1, 2</sup> It is a chronic disease of joint cartilage and bone and generally a disease of older individuals. Disease onset begins after age 40, with an estimated prevalence of 70% to 90% in people over the age of 75. Men and women are initially equally affected; after age 50, incidence is greater in women. Often symptoms appear earlier and can be more severe in women; moderate to severe radiographic OA is more prevalent in women than men for the hands, feet and knees (equal for hips). And, symptomatic OA prevalence is greater in women for hands, feet, knees and hips.<sup>3-6</sup> There is no known cure for the disease and current therapeutic strategies are directed at pain reduction and improvement of joint function.<sup>7,8</sup> OA is a leading cause of disability in the workplace, particularly in people over the age of 55.<sup>1,9</sup>

Osteoarthritis can be idiopathic (localized or generalized) or secondary to trauma (congenital, metabolic, endocrine, neuropathic or other medical causes).<sup>1</sup> The exact etiology of the pathology is

unknown, but involves the complex interplay of biomechanics, genetics and biochemicals. <sup>10, 11</sup> OA is characterized clinically by joint pain, swelling and functional limitations/stiffness and most commonly affects the knees, hips, hands and spine. Radiographically, it is characterized by osteophytes, bony sclerosis and joint space narrowing, and histopathologically, there are alterations in cartilage and subchondral bone integrity. 10 Modifiable risk factors for OA are weight, highimpact repetitive activities, and osteoporosis. Increased weight is the most significant independent predictor of both incidence and progression of OA in weight-bearing joints. Studies have demonstrated that weight reduction can reduce the development and progression of OA of the knee. 11 Maintaining an appropriate body weight may be the most important factor in preventing OA from occurring in weight-bearing joints. 11-13 In order to label osteoarthritis as "idiopathic," causes need to be considered and ruled out. These include but are not limited to: rheumatoid arthritis, lupus/other autoimmune arthritides, Wilson's disease, hemochromatosis, Paget's disease, septic arthritis, gout, and diabetic arthropathy. OA is classically associated with the absence of rheumatoid factors and with normal levels of acute phase reactants. However, rheumatoid factors may be present, usually in low titer, consistent with a person's advancing age. In addition, the erythrocyte sedimentation rate (ESR) and serum C-reactive protein concentration may be somewhat elevated, this is usually secondary to an associated disease. New markers which may be prognostic for progression of disease risk are on the horizon.<sup>14</sup>

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a validated instrument for the assessment of pain, stiffness, and physical function in patients with OA of the knee or hip. It assesses patients using 24 parameters and is particularly useful to monitor the course of the disease or to determine the effectiveness of therapeutic modalities. It tends to be used in the research arena, but is a very useful tool for evaluating the status of OA patients. The American College of Rheumatology has clinical classifications for hand, hip and knee OA, as well.

For our population of aviators, the major joints of concern with OA are the neck, spine, hands knees, and hips. Arthritis in the neck, spine and hands can be especially problematic in fighter/ ejection seat aircraft as well as for helicopter aircrew and for boom operators. Risk factors for OA of the knee include obesity, knee injury, previous knee surgery, and occupational bending and lifting. For OA of the hip, the risk factors include older age, high bone mass, genetic predisposition, increased BMI, participation in weight-bearing sports, and occupations that require prolonged standing, lifting, or moving of heavy objects. <sup>17</sup>

The diagnosis of OA is mainly clinical. The main symptoms/signs that suggest the diagnosis are pain, stiffness, reduced movement, swelling, crepitus, age greater than 40, and the absence of systemic features such as fever. Joint involvement is usually symmetric and morning joint stiffness that resolves within 30 minutes or occurs with mild-to-moderate activity is also common. With disease progression, more prolonged joint stiffness and joint enlargement becomes evident. Crepitus in the joint is a late manifestation of disease. Radiographic findings consistent with OA include presence of joint space narrowing, osteophyte formation, pseudocyst in subchondral bone, and increased density of subchondral bone. The absence of radiographic changes does not exclude the diagnosis of OA.

Treatment modalities include nonpharmacologic, pharmacologic and surgery. <sup>18</sup> Surgical intervention will not be covered in this waiver guide. The pharmacologic modalities can be analgesics, anti-inflammatory agents, intra-articular agents and the use of glucosamine with

chondroitin. With most OA patients, acetaminophen is the drug of choice; it can be used safely in doses up to 3g/day in patients not using other liver-metabolized medications or alcohol. Occasionally, the pain may be severe, and in those cases, the use of opioid analgesics such as codeine can be used, but should be avoided for long-term use. Non-steroidal anti-inflammatory agents (NSAIDs), such as ibuprofen, are commonly used. There is no convincing evidence that any of the available NSAIDs is more effective than any other for OA of the hip or knee. In comparing acetaminophen with NSAIDs, there is evidence that NSAIDs are superior to acetaminophen in terms of pain reduction and improvements in patient and physician global assessments and functional status. The relative superiority of NSAIDs over acetaminophen is most marked in those with moderate to severe levels of pain. The benefits of NSAIDs over acetaminophen are relatively modest, and therefore, additional factors are still important to consider in the decision to use these drugs. On the consider in the decision to use these drugs.

There has been considerable discussion over the past several years concerning the use of natural substances, glucosamine and chondroitin, for the treatment of OA. It has been touted to relieve symptoms and stop the disease progression, however data in the past failed to prove convincingly that it works, how it works, or whether it is even safe to take long-term.<sup>20</sup> Recent analysis showed the combination of glucosamine and chondroitin was non-inferior to celecoxib after 6 months of use and there were few risks from its use.<sup>21</sup> This natural combination therapy may be appropriate for a patient desiring to avoid acetaminophen or NSAIDs, but is not recommend for initial treatment.

Intra-articular corticosteroids can be very useful in OA patients who have pain despite appropriate dosing of an NSAID. Repeated injections over a period of up to two years appear to be safe and can be very effective. <sup>19</sup> In addition, hyaluronic acid injections have been used with some degree of success in certain sub-populations. Randomized trials have shown success in OA of the ankles, shoulders, and hips. Multiple injections are required with approximately five injections necessary for adequate treatment; one injection weekly for five weeks. The exact mechanism of action is unknown, but there may be a combination of an anti-inflammatory effect, a local lubricant effect, and an analgesic effect by direct buffering of synovial nerve endings. <sup>18</sup> With any intra-articular injection, the aviator needs to be placed in a DNIF status until the treatments are completed and the disease symptoms have improved.

The major nonpharmacologic entities include weight loss, rest, physical therapy, and exercise. Obesity and weight reduction are important, as noted above. Resting of the affected joint often alleviates pain, but prolonged rest may lead to muscle atrophy and decreased joint mobility. Physical therapy can improve flexibility and strengthen muscles supporting affected joints, and this often improves functional outcome and pain scores. In addition, there has been much discussion concerning orthoses, particularly for patients with OA of the knee. Research has suggested that neutral or laterally wedged shoe orthoses may be beneficial in the management of medial knee OA when used with walking shoes. Lastly, most recent studies support an appropriate exercise program as an integral part of the management of OA. Exercise goals are to reduce pain and functional impairment, protect involved and at-risk joints, and to prevent disability related to a more inactive lifestyle. Use of heat and cold packs, as well as, topical capsaicin may be incorporated into the therapeutic regimen. Overall, pain and functional status of OA (especially of the hip and knee) seems to deteriorate slowly, and there is limited evidence of OA worsening after 3 years of follow-up; so, ultimately, any type of exercise program that is done regularly and monitored by health professionals is essential to improving activities of daily living and function. 18, 25

### IV. Aeromedical Concerns.

The major concerns with aviators with OA are: distracting pain and joint limitations that may interfere with normal flight duties and with emergency egress activities. The chronic use of medications is of concern since it indicates ongoing pain; and the particular agents used to mitigate pain may result in other adverse aeromedical sequelae such as peptic ulcer disease, gastrointestinal bleeding, hepatic insufficiency, renal insufficiency or nephrolithiasis, altered mentation, sedation, etc. Acetaminophen and NSAIDs use can be waived on a regular basis, but use of opioid analgesics is not approved for aviation duties. If the aviator is using chronic NSAIDs, there must be regular follow-up with a CBC and BUN/Cr, and if using acetaminophen, to follow LFT level, and based on manufacturer recommendations.<sup>26</sup>

| ICD-9 codes for osteoarthritis |                                     |  |
|--------------------------------|-------------------------------------|--|
| 715                            | Osteoarthritis and allied disorders |  |
| 715.9                          | Degenerative Joint Disease          |  |
| 716.59                         | Polyarthritis                       |  |
| 716.9                          | Unspecified arthropathy, Arthritis  |  |

| ICD-10 codes for osteoarthritis |  |  |
|---------------------------------|--|--|
| M15.8                           | Other polyosteoarthritis                     |  |
| M19.90                          | Unspecified osteoarthritis, unspecified site |  |
| M13.0                           | Polyarthritis, unspecified                   |  |
| M12.9                           | Arthropathy, unspecified                     |  |

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#### WAIVER GUIDE

Updated: Mar 2015

Supersedes Waiver Guide of Feb 2012

By: Dr Dan Van Syoc

Reviewed by Lt Col Mark True, AF/SG consultant for Endocrinology

### **CONDITION:**

Osteoporosis/Osteopenia (Mar 2015)

### I. Waiver Consideration.

Osteoporosis or osteopenia is disqualifying for FC I/IA, II, III, and SWA duties. It is not listed as disqualifying for GBO or ATC, and is also not listed as disqualifying for retention purposes, unless the osteoporosis interferes with wear of required deployment equipment or requires ongoing specialist follow-up more than annually. If an underlying cause for osteoporosis was identified, the underlying disease must also be eligible for waiver. The finding of osteopenia or osteoporosis, whether or not of a degree that requires prophylaxis, may not require airframe restriction, but the occurrence of a fragility fracture would require restriction from high-performance and ejection seat aircraft. For FC III and SWA personnel, the variety of duties requires individual consideration; for instance, severe osteoporosis or the occurrence of a fragility fracture would contraindicate parachute duty.

Table 1: Waiver potential for osteoporosis and osteopenia

| Flying Class (FC) | Condition                   | Waiver Potential |
|-------------------|-----------------------------|------------------|
|                   |                             | Waiver Authority |
| I/IA              | Osteoporosis or Osteopenia  | Maybe            |
|                   |                             | AETC             |
| II/III/SWA        | Osteoporosis or Osteopenia  | Yes              |
|                   |                             | MAJCOM           |
| ATC/GBO           | Osteoporosis or Osteopenia* | N/A              |

<sup>\*</sup>Osteoporosis or Osteoporosis is generally not disqualifying for ATC and GBO personnel.

AIMWTS search in Jan 2015 revealed 65 cases with a diagnosis of osteoporosis or osteopenia. Of that total, 20 were disqualified. Breakdown was: 1 FC I case (disqualified); 33 FC II cases (10 disqualified); 27 FC III cases (8 disqualified); and 0 ATC/GBC cases, and 2 MOD cases (1 disqualified). About half of the cases were disqualified primarily due to the diagnosis of osteoporosis or osteopenia, and about 80% of the cases were on medication for the condition, the most common being Fosamax®.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for osteoporosis or osteopenia should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of the condition to include any falls, possible secondary causes, or any other metabolic conditions.
- C. Labs: Chemistry profile (electrolytes, blood urea nitrogen, creatinine, calcium, phosphorus, total protein, albumin, liver transaminases, and alkaline phosphatase), complete blood count, vitamin D level, and a 24-hour urine calcium
- D. Imaging: Bone density measurement (total hip and lumbar spine).
- E. RILO/MEB results if applicable.

The AMS for <u>waiver renewal</u> for osteoporosis or osteopenia should include the following:

- A. Interval history since last waiver
- B. Labs as above.
- C. Imaging: Bone density measurement (total hip and lumbar spine).

### III. Overview.

Osteoporosis is the most prevalent disease of bone, affecting an estimated 10 million Americans. <sup>1, 2</sup> It is a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and an increase in fracture risk, and is a major public health problem world-wide. <sup>3, 4, 5</sup> Osteoporosis is caused by a combination of increased bone resorption and inadequate bone formation which result in deterioration of trabeculae. <sup>6, 7</sup> Although it may be of clinical significance in men, osteoporosis is four times as common in women and is especially active in the first ten post-menopausal years. <sup>8, 9, 10</sup> Osteopenia is defined as low bone mass, but does not meet the diagnostic criteria of osteoporosis. These individuals are considered at an increased risk of developing osteoporosis in the future. <sup>11</sup> In the US, approximately 56% of all postmenopausal women have decreased bone mineral density (BMD), as measured at the hip, and 16% actually have osteoporosis. <sup>12</sup> Hip fractures, most of which are secondary to osteoporosis, cause an excess mortality of 10 to 20 percent at 12 months, and up to 25 percent of hip fracture patients require long-term nursing care. <sup>13</sup> Osteoporosis is estimated to impact around 14 million adults over the age of 50 in the US by the year 2020. <sup>4</sup>

The initial clinical presentation of osteoporosis typically is a fracture which may be symptomatic or occult. In the latter case, the typical finding is one or more spinal compression fractures on radiographs taken for other reasons. Fractures (especially hip, forearm, and spine fractures) also account for most of the morbidity of the disease, which is further complicated in many cases by subsequent poor healing. It is important to perform a diagnostic evaluation and to develop a prevention plan for these patients because a second hip fracture or a fragility fracture at another site is likely to occur. Consequently, patients may have chronic pain, postural/skeletal deformities, and in advanced cases restricted respiratory function from thoracic deformities. In the elderly population, osteoporotic fracture of the hip is frequently a pre-terminal event. With occasional exceptions, most of these problems will occur after a normal flying career has ended, but the rapidity of bone loss immediately after menopause in women predisposed to osteoporosis means that prophylaxis concerns will routinely arise during a flying career.

Table 2. Clinical risk factors for osteoporosis<sup>14</sup>

Advancing age

Previous fracture

Glucocorticoid therapy

Parental history of hip fracture

Low body weight

Current cigarette smoking

Excessive alcohol consumption

Rheumatoid arthritis

Secondary osteoporosis (e.g., hypogonadism or premature menopause, malabsorption, chronic liver disease, and inflammatory bowel disease)

The commonest form of osteoporosis appears to be caused by low estrogen state (e.g., postmenopausal, bilateral oophorectomy); additional risk factors which increase the likelihood or severity are listed in Table 1. Osteoporosis may also be secondary to a variety of other medical conditions. Certain diseases like hyperthyroidism, hyperparathyroidism, hypogonadism, and Paget's disease, any of which might reasonably be encountered in an aviator, can cause or mimic osteoporosis. A number of other diseases are in the broader differential diagnosis, including acromegaly, Cushing's syndrome, osteomalacia, and malignancies such as lymphoma and multiple myeloma. Furthermore, the use of certain medications such as heparin, glucocorticoids, vitamin A, and chemotherapeutic agents may occasionally be complicated by bone loss. <sup>12</sup> Men have a lower incidence of osteoporosis than women and this is due to multiple factors to include larger bones in men, hormonal factors and vitamin D levels. <sup>15</sup> Young healthy males not predisposed to secondary osteoporosis may occasionally present with unexplained fractures that lead to a finding of osteopenia as seen in a 2008 report involving a high performance pilot. <sup>16</sup>

To identify osteoporosis before fractures occur, screening for this disease is important. Current guidelines from the National Osteoporosis Foundation, the American Association of Clinical Endocrinologists, the National Institutes of Health, the U.S. Preventive Services Task Force and others agree that women greater than 65 years old, women with a history of postmenopausal fracture, or any adult with a fracture occurring in the absence of sufficient trauma should be screened for osteoporosis. Recently revised guidelines also recommend that postmenopausal women with risk factors for fracture be considered candidates for screening.

In the USAF aviator population, one is most likely to encounter perimenopausal women with concerns driven by a family history of postmenopausal osteoporosis. Consensus on how to proceed in this population has not been reached. However, a 43-year-old, Caucasian female weighing 120 pounds with irregular menstrual cycle and a family history of osteoporosis may benefit from screening and, if appropriate, treatment. The health care provider must exercise clinical judgment on individual assessments.

Dual-energy x-ray absorptiometry (DEXA or DXA Scan) is the most popular method of densitometry and is readily available in most medical communities for osteoporosis screening. DEXA scan results have been well-correlated with fracture risk. The results of a DEXA scan are reported using T-scores and Z-scores. T-scores are standard deviations from a normal young healthy population mean. Z-scores are standard deviations from an age-matched, sex-matched, and

sometimes race-matched population mean. Women with a T-score of -2.5 or lower (i.e., a larger negative number) are said to have osteoporosis, and those with a T-score between -1.0 and -2.5 are said to have osteopenia. Osteopenia should not be thought of as a separate disease, but an early form of osteoporosis, with the significant caveat that some women in the osteopenic range may not progress to osteoporosis.<sup>17</sup>

In addition to bone densitometry, laboratory screening for underlying causes of osteopenia and osteoporosis has also been widely supported, although a precise algorithm has not been uniformly endorsed. The utility of a workup depends on the clinical scenario. A reasonable approach would be to evaluate individuals initially diagnosed with osteoporosis with a complete blood count, serum chemistries (electrolytes, blood urea nitrogen, creatinine, calcium, phosphorous, total protein, albumin, liver transaminases and alkaline phosphatase), 25-hydroxyvitamin D levels, urinalysis, and 24-hour urine for calcium excretion and creatinine. Additional studies should be driven by history and clinical exam and may include thyroid function tests, parathyroid hormone, serum testosterone (men), serum estradiol, urine free cortisol, or others. For individuals who fail to respond to alendronate therapy, biochemical markers of bone metabolism (e.g., urinary N-telopeptide crosslinks) can be evaluated.<sup>7</sup>

Current strategies in osteoporosis treatment are increasingly focusing on preventing and mitigating the loss of bone in the post-menopausal women, and therapy is generally tailored to the bone density as determined by DEXA scan. All women can probably benefit from a healthy diet high in calcium, supplementation with calcium and with vitamin D, smoking cessation (when applicable), moderation of alcohol (if consumed), and regular weight-bearing exercise of any intensity.<sup>6</sup>

The American Association of Clinical Endocrinologists (AACE) has endorsed the National Osteoporosis Foundation Clinician's Guide to Prevention and Treatment of Osteoporosis.<sup>18</sup> Pharmacologic treatment for postmenopausal women is recommended for the following:

- o A hip or spine fracture (either clinical spine fracture or radiographic fracture).
- o A T-score of -2.5 or below at the spine, femoral neck, or total hip.
- A T-score between -1.0 and -2.5 at high 10-year risk of fracture with use of the US-adapted FRAX tool provided by the World Health Organization at <a href="https://www.shef.ac.uk/FRAX">www.shef.ac.uk/FRAX</a>, where treatment is considered cost-effective if the 10-year risk is 3% or more for hip fracture or 20% or more for 'major' osteoporosis-related fracture (humerus, forearm, hip, or clinical vertebral fracture)."11

Both hormone replacement therapy (HRT), with estrogen alone or combined with a progestin, and bisphosphonates have been considered first-line therapies for the management and treatment of osteoporosis. However, recent results from the Women's Health Initiative have raised concerns about breast cancer and cardiovascular risks due to HRT. For this reason, bisphosphonate therapy is the preferred first-line therapy in most cases. <sup>11, 19</sup>

Alendronate is a bisphosphonate approved by the US Food and Drug Administration (FDA) for the prevention and treatment of osteoporosis in postmenopausal women and is on the Official Air Force Approved Aircrew Medication List. Common side effects of alendronate for which aircrew should be monitored when using this medication include thoracic and abdominal pain (due to esophageal or gastric ulcerations), nonspecific gastrointestinal symptoms (nausea, vomiting, diarrhea, constipation), melena, hematochezia, musculoskeletal pain, headache, and allergic reaction. These

risks are minimized by technique of administration, which is outlined below.<sup>20</sup> Teriparatide (Forteo®), a recombinant parathyroid hormone, is also available; unlike bisphosphonate therapy, this agent consistently induces regrowth of bone. Major disadvantages of parathyroid hormone, besides expense and the necessity for refrigeration, include consistent elevations of serum calcium (with excursions into the abnormal range about 11% of the time), and the risk of inducing osteosarcoma. This agent is usually reserved for those with progressive failure of bisphosphonates, and for those with extreme levels of osteoporosis, and as such is rarely indicated. Therapy with teriparatide is not waiverable. Calcitonin therapy is very rarely employed; the usual indication is pain control in the face of recurrent fragility fractures, and thus neither the condition nor the therapy would be waiverable.<sup>17</sup>

Monitoring the efficacy of osteoporosis treatment is medically and aeromedically important, though there is some disagreement on how to monitor appropriately. The commonly accepted method to monitor sufficiency of treatment is to repeat bone densitometry at two year intervals. 11 Some patients will experience an increase in bone density on bisphosphonate therapy, but in general treatment is considered satisfactory if it results in arrest of bone loss. DEXA scanning should include the lumbar spine and bilateral hips. While bone density measurement of the left hip can be acceptable for making the diagnosis of osteoporosis, assessment of therapy requires serial measurement of lumbar spine and total hip scores. The lumbar spine value is based on AP lumbar spine, not the lateral. (The same is true for initial diagnosis; unlike the left hip T-score, the lateral spine T-score is not useful for diagnosis either.) Absolute BMD, rather than T-score, is assessed for response to therapy; a loss of 4% of hip density, and/or 5% of spine density, is considered significant. If this happens despite alendronate therapy, work-up should address poor absorption of the drug, and include re-evaluation of vitamin D levels. Finally, some investigators have advocated for the use of biochemical markers of bone turnover to monitor effectiveness of medical therapy. Currently there is controversy on which marker to use and if they truly give useful information to guide therapy.<sup>22</sup>

### IV. Aeromedical Concerns.

While certain aviation career fields, such as loadmaster or aeromedical evacuation crewmembers, routinely involve weight bearing labor, any aircrew member may be called upon for physical exertion. All aircrew have the potential need to quickly egress their aircraft. In many cases the egress route may involve climbing up or down, with drops or falls of several feet, and may necessitate the rapid movement of heavy objects or assistance to other crew members. These conditions would further increase the likelihood of pathologic fractures in an osteoporotic aviator. Furthermore, a fracture while egressing emergently would pose an additional threat to the safety of the injured aviator and other aircrew by delaying evacuation.

In high-performance aircraft, aviators have a known, increased risk of cervical and lumbar injury due to the large forces experience in high "G" maneuvers. No body of data exists regarding the response of osteopenic/osteoporotic aviators in this environment due to a paucity of affected individuals who have been exposed, although anecdotal cases have certainly occurred (e.g., symptomatic vertebral fracture during initial centrifuge training in an osteoporotic male). It is almost certain that acceleration stresses on bone tissue weakened by osteoporosis would result in a higher incidence of these types of injuries. A fragility fracture occurring under high-G conditions could even result in a catastrophic mishap.

Alendronate is a reasonably effective drug, and the risk of side effects is minor as long as proper technique of administration is followed. It should be taken on a fasting stomach with water only, and no other food or beverage should be consumed for an hour after medicating to prevent inactivation of the drug. To avoid esophageal damage, an upright posture needs to be maintained for at least an hour after ingestion. (The drug's inactivation by food can be useful; to further avoid the risk of esophageal ulceration, and the need to continue remaining upright, individuals are typically advised to eat a snack or meal an hour after taking the drug.) In high-performance aircraft some concern exists about the risk of inducing regurgitation of gastric contents due to G-suit abdominal compression, negative G<sub>z</sub> forces, and reclined seating. In order to minimize this risk, it is recommended that high-performance aviators dose alendronate on a day when no flying is planned. If conflict with the flying schedule is unavoidable, the aviator should medicate at least 30-60 minutes prior to flying, and should eat a snack just before taking off, which will effectively neutralize any remaining drug.<sup>16</sup>

| ICD-9 codes for osteoporosis and osteopenia |              |  |
|---|--------------|--|
| 733.00                                      | Osteoporosis |  |
| 733.90                                      | Osteopenia   |  |

| ICD-10 codes for osteoporosis and osteopenia |   |  |
|--|---|--|
| M81.8  | Other osteoporosis without current pathologic |  |
|  | fracture                                      |  |
| M89.9  | Disorder of bone, unspecified                 |  |

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#### WAIVER GUIDE

Updated: Jun 2015

Supersedes Waiver Guides of Jul 2014 and May 2010

By: Dr. Terry Correll (ACS psychiatrist) and Dr Dan Van Syoc

Reviewed by Col Mark Hubner, psychiatrist and chief, and the entire ACS Neuropsychiatry Branch

team.

#### **CONDITION:**

Other Conditions that May Be a Focus of Clinical Attention (Jun 2015)

#### I. Waiver Consideration.

"Other conditions" are not specifically mentioned in Medical Standards Directory (MSD), but the problems that may arise such as worry, anxiety, anger, depression, guilt, somatization, and behavioral acting-out may indeed lead to the need for grounding or disqualification. The following may cover many such conditions: "Any psychiatric condition, or history thereof, which would interfere with AFSC-specific aviation, controller or special duty performance (such as claustrophobia)". In addition, ARMA unsat (or its equivalent) is disqualifying for all duty positions.

Additionally, there are numerous conditions listed in the Medical Standards Directory (MSD) Psychiatry and Mental Health section that do not have a corresponding waiver guide topic. If any of those conditions apply to the aviator under consideration for a waiver, the guidance in this chapter applies.

Before submitting the case for waiver consideration, the base-level flight surgeon must first discern whether the condition is unsuiting vs. unfitting for service. If the Airman requires a fit/unfit determination, the case needs MEB action; if the airman requires suited/unsuited determination, the case then needs consideration of an administrative separation or discharge via the chain of command.

Table 1: Waiver potential for "Other Conditions" Diagnoses

| Flying Class (FC) | Waiver Potential | ACS Evaluation/Review    |
|-------------------|------------------|--------------------------|
|                   | Waiver Authority |                          |
| I/IA              | Yes              | At the request of AETC   |
|                   | AETC             | -                        |
| II/II             | Yes              | At the request of MAJCOM |
| ATC/GBO/SWA       | MAJCOM           | _                        |

An AIMWTS search in Jun 2015 revealed 83 cases with a V-code diagnosis. There were 4 FC I cases (all disqualified), 21 FC II cases (6 disqualified), 33 FC III cases (21 disqualified), 17 ATC/GBC cases (16 disqualified), and 8 MOD cases (all disqualified). Most of the disqualified cases were due to a mental health disorder other than the V code with the exception of 9 cases that were disqualified for V62.2 (ARMA unsat).

# II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

# Medical Standards Directory (MSD) and the Waiver Guide addresses waiver evaluations

# Step 1 - Is the aviator ready for waiver submission?

| m<br>ca<br>so | waiver is submitted when 1) the member is asymptomatic and 2) nedications/psychotherapy treatment have been completed, as applicable to diagnostic attegory, for the specified time-frame below (Note: psychotherapy "booster sessions", and ometimes aeromedically-approved antidepressants, are permissible and often advisable after nitial symptom resolution): |
|---------------|---|
|               | 1 Year—Psychotic Disorders & Somatoform Disorders   |
|               | 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior  |
|               | Discretion of Flight Surgeon—Adjustment Disorders & "Other Conditions" requiring waiver   |
|               | For Traumatic Brain Injury cases, please refer to TBI Waiver Guide  |
|               | For aviators with any other psychiatric disorders, please refer to Medical Standards Directory (MSD) and ACS Waiver Guide   |
|               | be considered for an aeromedical waiver, any disqualifying condition must meet the ng criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg. 57-58):   |
|               | Not pose a risk of sudden incapacitation  |
|               | Pose minimal potential for subtle performance decrement, particularly with regard to the higher senses  |
|               | Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment  |
|               | If the possibility of progression or recurrence exists, the first symptoms or signs must be easily detectable and not pose a risk to the individual or the safety of others   |
|               | Cannot require exotic tests, regular invasive procedures, or frequent absences to monitor for stability or progression  |
|               | Must be compatible with the performance of sustained flying operations  |
|               | - Before beginning the Aeromedical Summary (AMS), the Flight Surgeon must obtain a Health consultation and ensure it contains the items specified below:  |
| Instru        | ctions for the Mental Health Provider   |
| Γhe me        | ental health evaluation must include a <u>comprehensive written report</u> addressing:  Consultation must address each criteria in Step 1B  |
|               | Clinical mental health history (description of symptoms, treatment modality, frequency and  |
|               | compliance with treatment, relevant personal and family history, and perceived impact on occupational duties)   |
|               |   |

|          | Medication history (dates of initial prescription and termination, reason for termination, dosage,   |
|----------|--|
|          | compliance, response, clinical course since termination)   |
|          | Laboratory results as appropriate to individual case (i.e., thyroid, liver function tests, drug screen,  |
|          | CDT, CBC, chemical profile) ** for alcohol cases, please comment on carbohydrate-deficient   |
|          | transferrin (CDT) results**  |
| Ш        | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input  |
|          | from line leadership, if possible, current state of any triggers for the mental illness)   |
|          | Current and past aviation related duties and any history of current and past occupational  |
|          | performance difficulties (to include perceived impact of mental health condition on performance of duties)   |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)  |
|          | Summary and interpretation of psychological/neuropsychological testing results (recommend  |
| Ш        | MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact the   |
|          | ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended   |
|          | neuropsychological tests.  |
|          | Current mental status  |
|          | Diagnosis  |
|          | Motivation to fly or engage in special duty operations (past and current)  |
|          | Recommendation for future psychological and medical treatment  |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)   |
|          | Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand for   |
|          | shipment to ACS Neuropsychiatry Branch   |
| Step 3 - | Items for the Flight Surgeon to include in the AMS:  |
|          | AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safety  |
|          | Summarize Mental Health history and focus on occupational impact   |
|          | ** If 2 or more months have passed since the comprehensive evaluation/report was completed,  |
|          | the flight surgeon should address how the member has done since and consult with the mental  |
| _        | health provider if the member has been seen at mental health since the evaluation**  |
|          | Medication history (dates of initial prescription and termination, reason for termination, dosage,   |
|          | compliance, response, clinical course since termination)   |
|          | Laboratory results as appropriate to individual case (i.e., thyroid, liver function tests, drug screen,  |
|          | CDT, CBC, chemical profile) ** for alcohol cases, please comment on carbohydrate-deficient   |
|          | transferrin (CDT) results**  Current psychosocial situation (marital and occupational interview with spaces/supervisor if  |
| Ш        | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if possible - please address current state of any triggers for the mental illness) |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)  |
|          | Current mental status  |
|          | Diagnosis  |
|          | Motivation to fly (past and current)   |
|          |  |

| es) |
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Please feel free to contact the ACS Neuropsychiatry Branch with questions: SSgt Krista Traut 798-2653, or Mr. John Heaton: 798-2766

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. If the "other condition" designation is an additional diagnostic code listed for completeness during the treatment of another disqualifying mental disorder, waiver action should be taken primarily in accordance with the requirements for the primary disqualifying diagnosis. If the "other condition" resulting in prolonged interference with duty stands alone or there is a miscellaneous disorder not elsewhere covered by a waiver guide topic, then the AMS for the initial waiver should include the following:

- A. Any pertinent social, occupational, legal, or financial information, as well as a good history of the particular stressor. A paragraph describing the rationale why the member should be safe to return to flying status especially if the situational stressor is not completely resolved or if it could reasonably be expected to recur.
- B. A recent mental health evaluation, to include all treatment notes from the treating mental health professional as well as an MEB-type narrative summary of the mental health record.
- C. Any psychological testing or evaluation reports that may have been done in the evaluation and treatment.
- D. A letter from the flier's supervisor rendering an opinion about the aviator's readiness to return to flying status.

### The AMS for a waiver renewal should include the following:

- A. History and assessment of recurrence during the intervening period between last waiver and current request. Include an assessment of any situational stressors that previously existed or new stressors and how they affect the individual at this point.
- B. A recent mental health evaluation, to include all treatment notes from the treating mental health professional, if the nature of the condition originally warranted such re-evaluation.

#### III. Overview.

DSM-5 covers "other conditions and problems" that may be a focus of clinical attention or that may otherwise affect the diagnosis, course, prognosis, or treatment of a patient's mental disorder. These conditions are presented in the DSM-5 with their corresponding codes from ICD-9-CM (usually V codes) and ICD-10-CM (usually Z codes). Conditions or problems may be coded as such if they are a reason for the current visit or they help to explain the need for a test, procedure, or treatment. They may be a stand-alone reason for a patient visit, they may result from another mental disorder, or they may precipitate or exacerbate a mental disorder. Such conditions/problems may also be included in the medical record as useful information on circumstances that may affect the patient's care, regardless of their relevance to the current visit. The conditions are broadly divided into Relational Problems, Abuse and Neglect, Educational and Occupational Problems, Housing and Economic Problems, Other Problems Related to the Social Environment, Problems Related to Crime or Interaction with the Legal System, Other Health Service Encounters for Counseling and Medical Advice, Problems Related to Other Psychosocial, Personal, and Environmental Circumstances, and Other Circumstances of Personal History. The DSM-5 greatly expanded upon the 23 "V codes" listed in the DSM-IV-TR.

Family and relational issues are common reasons for aviators to seek assistance. Marital relations have the strongest influence on health. The oft-used Holmes and Rahe scale demonstrates that 10 of the 15 most stressful events are family events. For example, divorce can have long-lasting effects on all members of a family. Multiple studies have indicated that divorce is more traumatic for boys than for girls in divorced families. Similarly, family environments that are characterized by verbal conflict or physical violence can have a negative impact on a person's psychosocial development. These negative influences can extend well into adulthood for both males and females.

Every aviator has unique experiential histories. How that person responds to the stressors of life is highly dependent on their home of origin and how they were conditioned as a child and adolescent. Similar stressors applied to multiple individuals will elicit a wide range of responses. We see this often after disasters and major accidents. Flight surgeons need to be aware of stressors in the lives of their aviators and pay close attention to the response to past and current stressors.

Previously there were several psychiatric diagnostic categories in the waiver guide which have since been removed. The reason for so doing is that there have been practically no AIMWTS submissions in these categories, and the few cases submitted had a strong predilection for a permanent disqualification or administrative/punitive separation from military service. Good initial screening of our aviation applicants significantly minimizes the chances of these individuals ever achieving flight status.

However, there are rare cases of aviators with a disorder that falls in one of such diagnostic categories (for example, Impulse Control Disorder, Psychological Factors Affecting Medical Conditions, and Sexual Dysfunction), or who have another miscellaneous condition not on the current waiver guide list, who will be successfully treated by mental health professionals and deemed cured or in a long-term state of remission. After a thorough evaluation it may be determined that the aviator is fit for waiver consideration.

#### IV. Aeromedical Concerns.

The "other conditions" represent a psychiatric gray area in aerospace medicine. Many of the everyday problems faced by flyers - and therefore by flight surgeons - may be described by these conditions. These involve the kinds of situations discussed in flying safety talks by flight surgeons, or in stress management lectures by aerospace psychologists or physiologists, because they may interfere with safe or effective flying. Matters such as adjusting to different cultures, dealing with a recalcitrant child, or trying to save a failing marriage are of obvious aeromedical concern, but whether they are grounds for administrative or medical removal from flying duties, or for establishing a psychiatric diagnosis, are clearly matters of degree. What becomes most relevant to aeromedical decision-making is the response of the aviator rather than the severity of the stressor. Numerous "small" stressors can produce as much fatigue, irritability, early task saturation, distraction, and cognitive inefficiency as a single major stressor.

Aeromedically dangerous responses to stressors include those of worry, anxiety, anger, depression, guilt, somatization, and behavioral acting-out. These responses may occur during stable situations, or during such contingencies as unexpected TDYs, deployments, or a PCS. Other aeromedically relevant issues include disruption of sleep, significant weight loss or gain, preoccupation, inability to relax, overall mood, affective changes, duty requirements, and especially flying performance as assessed by the flyer, peers, and the supervisor. Because these conditions and their impact can be insidious, the flight surgeon should approach such life problems in flyers carefully, using techniques that range from informal discussion, as the least intrusive intervention, all the way to a referral for full mental health workup/treatment. Each type of assessment or intervention should consider whether the aviator should continue to fly. In some cases, the aviator may be able to resolve the troubling issue without being placed in a DNIF status. If placed DNIF, once the flyer has completed use of any medications/psychotherapy, and the symptoms are sufficiently relieved so that return to flying is possible, then decide whether a waiver will be necessary. *Note: A flyer may be recommended for return to flying even though non-medication "talk therapy" is continuing when the symptoms have subsided sufficiently (during marital therapy, for example)*.

If the concerning responses to the stressor persist or are severe, a formal mental health diagnosis may be warranted. The flight surgeon must always be vigilant for more severe pathology. Relationship distress is a good example of a stressor that may precipitate multiple DNIF periods due to loss of sleep and evolve into an "other condition" requiring evaluation and treatment. It may be that the relationship issue precipitates a Major Depressive Disorder that requires treatment and a waiver. The relationship problems may even be the result of a Major Depressive Disorder that began affecting the aviator's personal relationships. If a diagnosis seems warranted, establish it in accordance with DSM-5 criteria, and see that the flyer receives proper treatment. The length of demonstrated stability post-treatment prior to submission of a waiver is at the discretion of the flight surgeon. NOTE: Beware of delaying or withholding proper treatment solely in order to avoid DNIF or to "protect the aviator's career."

Most flyers with the more unusual mental health diagnoses typically have other concurrent emotional disturbances such as anxiety, depression, or substance abuse/dependence that may be aeromedically significant. Others have personality issues or traits that are problematic. Flyers with these unusual traits should be individually assessed with attention given to rule out a DSM-5 diagnosis.

Some of the diagnoses (primary such as an impulse control disorder or secondary such as antisocial personality traits/disorder) tie in closely with reliability, integrity, and security concerns. Returning these aviators to flight status may cause subsequent issues in the squadron and morale problems among the flight crew. Many of these individuals also have unstable interpersonal relationships with family which can have a significant negative impact on flying operations. Administrative, legal, or security clearance action may be required even if the primary problem is not medically disqualifying.

| ICD-9-     | ICD-10<br>Codes  |         |
|------------|--|---------|
| V62.3      | Academic or Educational Problem  | Z55.9   |
| V62.4      | Acculturation Difficulty   | Z60.3   |
| V71.0      | Adult Antisocial Behavior  | Z72.811 |
| V62.8<br>2 | Bereavement, Uncomplicated   | V62.82  |
| V61.0<br>3 | Disrusption of family by separation or divorce                           | Z63.5   |
| V62.2<br>2 | Exposure to Disaster, War, or Other Hostilities                          | Z65.5   |
| V61.8      | High Expressed Emotion Level Within Family                               | Z63.8   |
| V65.2      | Malingering  | Z76.5   |
| V15.8<br>1 | Nonadherence to medical treatment  | Z91.19  |
| V62.2<br>9 | Other problem Related to Employment                                      | Z56.9   |
| V62        | Other Psychosocial Circumstances   |         |
| 312.89     | Other specified disruptive, Impulse-Control, and Conduct Disorder        | F91.9   |
| 278.00     | Overweight or Obesity  | E66.9   |
| V61.2<br>0 | Parent-Child Relational Problem  | Z62.820 |
| -          | Personal history (past history) of neglect in childhood                  | Z62.812 |
|            | Personal history (past history) of physical or sexual abuse in childhood | Z62.810 |
|            | Personal history (past history) of psychological abuse in childhood      | Z62.811 |
| V62.8<br>9 | Phase of Life Problem  | Z60.0   |
| V62.2<br>1 | Problem Related to Current Military Deployment Status                    | Z56.82  |
| 316        | Psychological Factors Affecting Medical Conditions                       | F54     |
| V61.1<br>0 | Relationship Distress With Spouse or Intimate Partner                    | Z63.0   |
| V62.8<br>9 | Religious or Spiritual Problem   | Z65.8   |
| 302.70     | Unspecified Sexual Dysfunctions  | F52.9   |

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### Otosclerosis/Stapedectomy (Apr 2019)

Reviewed: Lt Col Ross Semeniuk (RAM 2020), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), Lt Col Wesley Abadie (AF/SG Otolaryngology Consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

Updated format

#### I. Waiver Consideration

Otosclerosis is an ankylosis involving the stapes footplate and the surrounding bone of the inner ear. Otosclerosis is addressed in the MSD and is disqualifying for all flying and special operational duties when it interferes with normal hearing.

There are various medical and surgical treatments that may be considered to address the condition. The most common surgical procedures are a total or partial stapedectomy, or stapedotomy. In addition to meeting the audiology standards, an ACS review is required for flying class I/IA and class II single seat high performance aviators following stapes surgery.

**Table 1: Waiver potential for Otosclerosis** 

| Flying Class (FC) | Waiver Potential | ACS Review/Evaluation                 |
|-------------------|------------------|---------------------------------------|
|                   | Waiver Authority |                                       |
| I/IA              | Yes <sup>2</sup> | ACS review necessary if               |
|                   | AETC             | stapes surgery performed              |
| II/III/SWA        | Yes <sup>2</sup> | ACS review necessary if               |
|                   | MAJCOM           | stapes surgery performed <sup>1</sup> |
| ATC/GBO           | Yes <sup>2</sup> | No                                    |
|                   | MAJCOM           |                                       |

<sup>1.</sup> Single seat high performance aircrew only.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment for all clinical diagnoses.
- 2. Complete history to include all hearing and vertiginous symptoms along with impact on activities of daily living and aviation duties. Discuss all attempted treatments (e.g. hearing aids).
- 3. Otolaryngologist and audiologist consultation reports, including follow-up notes with examination findings after disease resolution.
- 4. Complete audiologic exam to include:
  - a. Air conduction threshold measurement;
  - b. Bone conduction threshold measurement (if indicated);

<sup>2.</sup> No indefinite waivers.

- c. Speech reception threshold;
- d. Speech discrimination testing;
- e. Acoustic impedance testing; and
- f. ENG if clinically indicated.
- 5. All surgical reports to include:
  - a. Details of technique used,
  - b. Type of prosthesis; and
  - c. Type of graft used.
- 6. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 7. Any other pertinent information.
- 8. If the above items are not available, it is necessary to explaining reasoning to the waiver authority.

# B. Renewal Waiver Request:

- 1 If any abnormalities surface in the interim, they will need to be addressed appropriately.
- 2 Interim history to include any change in hearing, any side effects such as vertiginous symptoms, and any operational issues.
- 3 Exam: Otolaryngology and audiology evaluations.
- 4 If the above items are not available, it is necessary to explaining reasoning to the waiver authority.

#### III. Aeromedical Concerns

The chief aeromedical concerns relate to progressive hearing loss. In addition, otosclerosis may result in vestibular symptoms significant enough to impact flight safety.

Most aviators will present with a chief complaint of hearing loss as the pathologic process affects the speech range frequencies. Although it is important to consider the impact of Paracusis of Willis – improved perception of speech in a noisy environment, hearing loss will eventually impair communication leading aviators to seek surgical or audiometric remediation. Corrective surgery is highly successful in restoring the aviator's auditory acuity. However, there are post-operative risks, which although rare, include; injury to the facial nerve, inner or middle ear infection, meningitis, disturbances of equilibrium, conductive hearing loss, persistent perforation of the tympanic membrane, and perilymph fistula – each of which may prevent the proper use of safety equipment or cause incapacitation through loss of hearing or situational awareness.

At one time, it was controversial whether to provide waivers post-stapedectomy. Fortunately, the majority of known complications to stapes surgery become evident within the first one or two months following the procedure. Only disturbances in equilibrium and delayed sudden hearing loss are believed to present beyond the first few weeks, although there are reports of chronic perilymph fistulas. The latter is the most serious long-term complication for aviators. On account of extensive post-operative data and altitude chamber experience, there is consensus that after an appropriate waiting period to rule out immediate post-operative complications, return to flying status after stapedectomy can be both safe and responsible.

A Feb 2019 review of AIMWTS revealed 52 cases submitted for a waiver with the diagnosis of otosclerosis. This total included 1 FC I case, 31 FC II cases, 17 FC III cases, 2 ATC/GBC cases, and 1 MOD case; all received a waiver except 1 FC II and 1 FC III.

| ICD-9 codes for Otosclerosis and Stapedectomy |                           |  |
|---|---------------------------|--|
| 387   | Otosclerosis              |  |
| 387.9   | Otosclerosis, unspecified |  |
| 19.1  | Stapedectomy              |  |
| 19.19   | Other stapedectomy        |  |
| 19.9  | Stapedotomy               |  |

| ICD-10 codes for Otosclerosis and Stapedectomy |                                     |  |
|--|-------------------------------------|--|
| H80.83   | Other otosclerosis, bilateral       |  |
| H80.93   | Unspecified otosclerosis, bilateral |  |
| Use ICD-9                                      | Stapedectomy                        |  |
| Use ICD-9                                      | Other stapedectomy                  |  |
| Use ICD-9                                      | Stapedotomy                         |  |

## **IV. Suggested Readings**

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### **WAIVER GUIDE**

Updated: Jan 2017

Supersedes Waiver Guide of Jul 2013

By: Maj M. Bradley Brough (RAM 18) and Dr. Dan Van Syoc

Reviewed by Col Pat Storms, RAM 2005 and AF/SG consultant for Gastroenterology

### **CONDITION:**

Pancreatitis (Jan 2017)

#### I. Waiver Consideration.

Pancreatitis, regardless of the etiology, is disqualifying for all classes of flying in the USAF. If the diagnosis of pancreatitis does not meet retention standards per the MSD (chronic, recurrent, complicated, etc.), then a waiver is required for ATC/GBO or SWA cases.

**Table 1 – Waiver Potential for Pancreatitis** 

| Flying Class | Condition | Waiver Potential | ACS Evaluation or    |
|--------------|-----------|------------------|----------------------|
| (FC)         |           | Waiver Authority | Review               |
| I/IA         | Acute     | Yes*             | If requested by AETC |
|              |           | AETC             |                      |
|              | Chronic   | No               | No                   |
|              |           | AETC             |                      |
| II/III       | Acute     | Yes*             | If requested by      |
|              |           | MAJCOM           | MAJCOM               |
|              | Chronic   | Yes*+#           |                      |
|              |           | AFMSA            | Yes                  |
| ATC/GBO      | Acute     | N/A              | No                   |
| SWA          |           |                  |                      |
|              | Chronic   | Yes*+#           | No                   |
|              |           | AFMSA            |                      |

<sup>\*</sup> Waiver possible with resolution of the acute phase and no sequelae from chronic state.

A review of AIMWTS in Jan 2017 revealed 80 dispositions for pancreatitis with 12 of them resulted in disqualification. There were 8 FC I/IA cases (1 disqualified), 38 FC II cases (3 disqualified), 32 FC III cases (8 disqualified), 1 ATC/GBC (0 disqualified) cases, and 2 MOD cases (0 disqualified). Of the 12 DQ cases, 4 were for EtOH or substance abuse, 3 were related to the diagnosis of pancreatitis, and 5 for another medical problem.

<sup>+</sup> MEB required prior to waiver consideration.

<sup>#</sup> No indefinite waiver.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

### Acute pancreatitis (All flying classes):

The AMS for acute pancreatitis should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. A complete discussion of the history and etiology of the condition and how it was treated.
- C. A statement that the aviator is completely recovered from the illness, that he/she has not suffered any complications, and that he/she is tolerating a regular diet, and is capable of normal activities.
- D. Consultation report by a gastroenterologist specifically addressing the likelihood of recurrence.
- E. Documentation:
  - Reports: Operative reports, consultation reports, hospital discharge summary.
  - <u>Imaging studies</u>: Post-recovery abdominal CT scan (demonstrating a healthy pancreas without pseudocyst or calcifications), and an ultrasound or other study demonstrating the absence of gallstones or sludge.
  - <u>Lab studies</u>: CBC, glucose, calcium, amylase, lipase, trypsin, fasting lipid panel, and liver function tests.

## Chronic pancreatitis:

Active chronic pancreatitis is not waiverable. Patients with a history of chronic pancreatitis, who are currently asymptomatic with no sequelae such as chronic diarrhea, chronic pain, or diabetes mellitus, may be considered for a waiver following MEB with a "return to duty" recommendation. Patients with a history of surgical interventions for chronic pancreatitis, such as segmental pancreas resection or Puestow procedure are unlikely to be considered for waiver, and would have to demonstrate complete functional recovery post operatively with no sequelae from the surgery or chronic pancreatitis prior to any waiver consideration.

<u>Waiver Renewal</u>: For a time limited waiver, a renewal aeromedical summary is needed. It should include all interim history and medical information necessary to update the case.

### III. Overview.

Pancreatitis is a condition in which digestive enzymes are activated within the pancreas instead of the small intestine, causing organ injury with a significant and damaging inflammatory response in the pancreas.<sup>1</sup> The disease can present as either an acute or chronic condition.

Acute pancreatitis has an incidence of 70-80 per 100,000 people in the United States and accounts for more than 200,000 hospital admissions annually.<sup>2,3</sup> Symptoms typically include an abrupt onset of constant, dull, posteriorly radiating abdominal pain (due to the retroperitoneal location of the pancreas), nausea and vomiting.<sup>1</sup> The physical exam will generally reveal an anxious patient in some distress with tachycardia, low-grade fever, hypotension and reluctance to lay supine since that position stretches the pancreas and increases pain. The abdomen may be diffusely tender and rigid with diminished bowel sounds. Lab abnormalities may include leukocytosis, elevated amylase and lipase (greater than 3 times the upper limit of normal), hyperglycemia, hypocalcemia, elevated liver

function tests, elevated C-reactive protein or Neutrophil–Lymphocyte Ratio (NLR), hypertriglyceridemia (in cases where elevated triglycerides are the cause of the problem), hemoconcentration, and hypoxia.<sup>3,4,5</sup> Imaging tests include chest and/or abdominal x-ray, ultrasound and CT scan which can be used to not only diagnose pancreatitis, but also to assess the severity and predict complications of acute pancreatitis.<sup>6</sup> Additionally, magnetic resonance cholangiopancreatography (MRCP) may be used because of its ability to detect choledocholithiasis down to 3 mm in diameter, visualize the pancreatic duct and its safer use in contrast allergy and renal insufficient patients.<sup>7</sup>

The etiology of acute pancreatitis can be due to numerous causes, but approximately 40% of cases result from cholelithiasis (or microlithiasis with stones <5 mm in size) and 35% from heavy alcohol use.<sup>3</sup> Of note, pancreatitis due to alcohol abuse develops after four to seven years of drinking and can have a more gradual onset of abdominal pain than the abrupt pain associated with cholelithiasisinduced pancreatitis.<sup>2</sup> Additionally, pancreatitis can be caused by trauma (especially abdominal) or can present as a postoperative complication. Metabolic causes include acute fatty liver of pregnancy, hypertriglyceridemia (2-4% of pancreatitis cases), and hypercalcemia. If hypercalcemia is present, consider the diagnosis of hyperparathyroidism. Rare metabolic causes include apolipoprotein CII deficiency. Infectious causes include mumps, viral hepatitis, ascariasis, mycoplasma, campylobacter, M. avium complex, and a variety of viruses, such as coxsackievirus, echovirus and cytomegalovirus. Any condition that obstructs the ampulla of Vater can cause pancreatitis, such as a duodenal diverticulum, regional enteritis as well as neoplasms such as pancreatic cancer and other masses. Endoscopic retrograde cholangiopancreatography (ERCP) is an increasing cause of disease with estimates of 1-4% of all attributable cases linked to this procedure.<sup>3</sup> A variety of medications are also known to cause pancreatitis. These include sulfonamides, oral contraceptive pills and other estrogens, tetracycline, thiazide diuretics, azathioprine, furosemide, valproic acid, acetaminophen, nitrofurantoin, erythromycin, salicylates, metronidazole, NSAIDs, ACE inhibitors, and methyldopa. Connective tissue disorders that cause vasculitis may also cause pancreatitis; these include systemic lupus erythematosus, necrotizing angiitis and thrombotic thrombocytopenic purpura. Additionally, pancreatitis can be a complication of a penetrating peptic or duodenal ulcer. Pancreatitis can be hereditary, caused by carrying the cystic fibrosis gene or by a mutation in the trypsinogen gene, and can be caused by congenital malformation of the pancreas. Finally, pancreatitis is idiopathic in approximately 15-20% of cases. If pancreatitis is recurrent and no obvious cause is found, consider occult biliary disease, neoplasm, cystic fibrosis, hypertriglyceridemia, sphincter of Oddi dysfunction, or pancreas divisum. Clinicians treating patients with acute pancreatitis need to recognize that the disease is dynamic and the severity and symptoms often change during the course of the disease.<sup>8</sup>

Chronic pancreatitis results from recurring, progressive pancreatic inflammation leading to permanent organ damage, and loss of endocrine and exocrine function. <sup>9</sup> It has an incidence of about 3-10 per 100,000. The most common cause is alcohol abuse. CT findings show parenchymal loss and calcifications within the pancreas. Additionally, cystic fibrosis, hypertriglyceridemia, hemochromatosis, severe malnutrition, gastric surgery or pancreatic resection, neoplasm of the pancreas or duodenum, gastrinoma, and abdominal radiation therapy can all cause chronic pancreatitis. Chronic pancreatitis may also be idiopathic or hereditary. A rare cause is alpha-1 antitrypsin deficiency. Chronic pancreatitis usually presents with chronic pain, malabsorption with malnutrition, weight loss, steatorrhea, or gastroparesis. Complications may include narcotic addiction, diabetes mellitus, pancreatic cancer, and permanent pancreatic insufficiency.<sup>2</sup>

Treatment of acute pancreatitis is generally supportive and includes pain control and aggressive IV fluid replacement.<sup>3, 6, 10</sup> Current recommendations for hydration are 250-500 mL per hour of isotonic crystalloid solution for the first 12-24 hours for all patients unless cardiovascular, renal or other comorbidities exist (fluid requirements should be assessed frequently throughout the first 24 hours).<sup>6</sup> The topic of nutritional support in acute pancreatitis is not without controversy. Recommendations for gut rest conflict with recent recommendations to pursue enteral nutrition via nasogastric or nasojejunal routes.<sup>6,11</sup> While prophylactic antibiotics are not recommended, infected necrosis should drive the use of antibiotics and percutaneous drainage in a "step up" approach.<sup>3, 6, 11</sup> If the etiology of acute pancreatitis is cholelithiasis then laparoscopic cholecystectomy may be indicated, as early cholecystectomy has been shown to decrease complications in those with gallstone pancreatitis.<sup>6, 12</sup> Urgent ERCP is strongly recommended within the first 24 hours in patients who have severe biliary pancreatitis with organ failure or cholangitis.<sup>6, 11</sup> Chronic pancreatitis may require pancreatic enzyme replacement as well as pain control and management of its complications. Occasionally, chronic pancreatitis can be relieved by endoscopy or surgery to open the sphincter of Oddi or by removing part of the pancreas.<sup>9</sup>

### IV. Aeromedical Concerns.

Acute pancreatitis is disqualifying if the case is complicated or associated with large persistent pseudocysts. Pancreatitis that is chronic or recurrent is also disqualifying. In both types of disqualifying pancreatitis, it is so for all flying classes, ATC/GBO, and SWA personnel, as well as for retention purposes. Any acute pancreatitis, or history of pancreatitis, is also disqualifying for IFCI/IA, FCII, RPA Pilot and FCIII.

Acute pancreatitis can be sudden and devastating in its onset, and as such, it poses a danger to flight and to mission completion. The complications of chronic pancreatitis such as chronic pain, diabetes, pancreatic cancer, and the drugs required to treat those complications, likewise endanger flying safety and mission completion. Furthermore, the underlying cause of the pancreatitis (such as alcohol abuse) may pose a serious danger to the safety of flight.

The flight surgeon must determine if the underlying cause of the pancreatitis is waiverable in its own right (refer to the Medical Standards Directory and AF Waiver Guide). For example, alcohol abuse complicated by pancreatitis is generally not waiverable; cholelithiasis corrected by surgery is waiverable. If the cause was a medication, the aviator must be switched to a drug that is waiverable (and the pancreatitis must resolve without sequelae). It is important to caution the patient to NEVER use the offending drug in the future. If the underlying cause requires a Medical Evaluation Board (MEB), that must be accomplished prior to requesting a waiver. Waivers for pancreatitis caused by cholelithiasis will not be considered unless the gallbladder has been removed, after which an indefinite waiver is possible. Waivers for hereditary pancreatitis or pancreatitis due to uncorrectable factors will generally not be considered. If the pancreatitis was caused by binge drinking, the flyer must have undergone an ADAPT evaluation demonstrating that he or she is not an alcoholic and that he or she has gone through alcohol counseling and education.

| ICD-9 Codes for Pancreatitis |                      |
|------------------------------|----------------------|
| 577.0                        | Acute pancreatitis   |
| 577.1                        | Chronic pancreatitis |
| 072.3                        | Mumps pancreatitis   |

| ICD-10 Codes for Pancreatitis |                                 |
|-------------------------------|---------------------------------|
| K85.9                         | Acute pancreatitis, unspecified |
| K86.1                         | Other chronic pancreatitis      |
| B26.3                         | Mumps pancreatitis              |

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#### WAIVER GUIDE

Updated: Mar 2016

Supersedes Waiver Guide of June 2012

By: Lt Col Tracy Bozung (RAM 17) and Dr. Dan Van Syoc

Reviewed by Col Pat Storms, AF/SG consultant for gastroenterology

### **CONDITION:**

Peptic Ulcer Disease (Mar 2016)

### I. Waiver Consideration.

Active peptic ulcer disease is disqualifying for all flying classes, ATC, GBO and SWA personnel. Resolved peptic ulcer disease that was complicated by hemorrhage, obstruction, or perforation is also disqualifying for all flying classes, ATC, GBO, and SWA personnel If the disease process leads to repeated incapacitation or absences from duty, or requires frequent specialty follow-up, it is also disqualifying for retention and an IRILO is required.

Table 1 – Waiver Potential for PUD for FC I/IA, FC II and FC III

| Flying Class      | Condition   | Waiver Potential  | ACS               |
|-------------------|---|-------------------|-------------------|
| (FC)              |   | Waiver Authority# | Review/Evaluation |
| I/IA              | Peptic ulcer disease,   | No                | No                |
| Initial II or III | active or refractory  | AETC              |                   |
|                   | Peptic ulcer complicated by hemorrhage, obstruction or perforation. | Yes*+<br>AETC     | Yes               |
| II/III            | Peptic ulcer disease,   | Yes*+#            | Yes               |
|                   | active or refractory  | MAJCOM            |                   |
|                   | Peptic ulcer complicated  | Yes*+#            | Yes               |
|                   | by hemorrhage, obstruction or perforation.                          | MAJCOM            |                   |
| ATC/GBO           | Peptic ulcer disease,   | Yes*+             | At MAJCOM         |
|                   | active or refractory  | MAJCOM            | request           |
|                   | Peptic ulcer complicated by hemorrhage, obstruction or perforation. | Yes*+<br>MAJCOM   | At MAJCOM request |

<sup>\*</sup> Waiver possible with documentation of treatment and resolution of symptoms or documentation of adequate control measures.

<sup>+</sup> MEB required first if individual experiences repeated incapacitations or absences from duty because of recurrence of symptoms despite good medical management which is supported by laboratory and/or X-ray evidence of activity or severe deformity.

<sup>#</sup> AFMRA is waiver authority if aviator does not meet retention standards or if limitation code C from MEB in place.

Review of AIMWTS in Mar 2016 revealed 77 waiver requests for peptic ulcer disease. Breakdown of the cases demonstrated 4 FCI cases, 30 FCII cases, 36 FCIII cases, and 7 ATC/GBC cases. Of the 77 cases, four (5.2%) were disqualified; one ATC/GBC and one FCIII were disqualified for unrelated medical issue (neck pain and IBS) and one FCIII and one FCIII were disqualified for multiple disqualifying conditions in addition to PUD.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for peptic ulcer, regardless of etiology, must include the following:

- A. History and physical with note of presence or absence of ulcer complications (obstruction, perforation, or bleeding), and NSAID, tobacco and alcohol use
- B. Documentation of *H. Pylori* status, treatment and eradication (as applicable)
- C. Documentation of cessation of NSAID use (as applicable)
- D. Documentation of ulcer healing by confirmatory endoscopy
- E. Report of current (returned to baseline) hemoglobin and hematocrit result
- F. Documentation that the aviator has been counseled about the warning symptoms of ulcer recurrence and complications (pain, melena, BRBPR, hematemesis, nausea and vomiting, lightheadedness, dyspnea on exertion)
- G. Documentation that the aviator is asymptomatic without acid-suppressing medication (waiver may be considered on a case-by-case basis with chronic acid suppression therapy)
- H. MEB results if aviator does not meet retention standards.

Recurrence risk of peptic ulcers without clear etiology is unknown. Waiver may be considered on a case-by-case basis.

#### III. Overview.

Peptic ulcer disease (PUD) is characterized by mucosal damage secondary to pepsin and gastric acid secretion, and is most often encountered in the stomach and proximal duodenum. Ulcers may also be found in the lower esophagus, distal duodenum, or jejunum in unopposed hypersecretory states such as Zollinger-Ellison syndrome, in hiatal hernias, or in ectopic gastric mucosa (e.g., in Meckel's diverticulum). The incidence of peptic ulcers is declining, possibly as a result of the increasing use of proton pump inhibitors and decreasing rates of *Helicobacter pylori* infection. <sup>2, 3, 4</sup>

*H. pylori* infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) are the predominant causes of peptic ulcer disease in the United States. Along with smoking, they account for 89% to 95% of PUD and related serious upper GI events.<sup>5</sup> A variety of other infections and comorbidities are associated with a greater risk of peptic ulcer disease (e.g., cytomegalovirus, tuberculosis, Crohn's disease, hepatic cirrhosis, chronic renal failure, sarcoidosis, myeloproliferative disorder). Critical illness, surgery, or hypovolemia leading to splanchnic hypoperfusion may result in gastroduodenal erosions or ulcers (stress ulcers); these may be silent or manifest with bleeding or perforation. Smoking also increases the risk of ulcer recurrence and

slows healing.<sup>6</sup> Among those patients not using NSAIDs, the incidence of PUD increases with age and is approximately two times more common in men.<sup>7</sup>

Although *H. pylori* is present in the gastroduodenal mucosa in most patients with duodenal and gastric ulcers, the majority of patients with *H. pylori* infection do not develop peptic ulcer disease. *H. pylori* bacteria in the gastric tract adheres to the gastric mucosa, beneath the protective mucus layer. The presence of an outer inflammatory protein and a functional cytotoxin-associated gene island in the bacterial chromosome increases virulence and probably ulcerogenic potential. 

Patients with *H. pylori* infection have increased resting and meal-stimulated gastrin levels, decreased gastric mucus production, and decreased duodenal mucosal bicarbonate secretion, all of which favor ulcer formation. Ulcer recurrence has been shown to be much less common in those patients who are *H. Pylori*-cured (6%) vs. non-cured (67%) in patients with duodenal ulcers and in patients with gastric ulcers, cured (4%) vs. uncured (59%). 

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Topical effects of NSAIDs cause submucosal erosions. In addition, by inhibiting cyclo-oxygenase, NSAIDs inhibit the formation of prostaglandins and their protective cyclo-oxygenase- 2-mediated effects (i.e., enhancing gastric mucosal protection by stimulating mucus and bicarbonate secretion and epithelial cell proliferation and increasing mucosal blood flow). Coexisting *H. pylori* infection increases the likelihood and intensity of NSAID-induced damage. As many as 25% of chronic NSAID users will develop ulcer disease and 2 to 4% of those patients will develop GI bleeding or perforation. NSAID use is responsible for approximately one half of perforated ulcers, which occur most commonly in older patients using chronic aspirin or other NSAIDs. Ameta-analysis in 2015 showed a 73% reduction in peptic ulcers with those patients taking a PPI with aspirin as compared to aspirin alone. There is also evidence that COX-2 inhibitors have a lower incidence of gastric and duodenal ulcers compared to traditional NSAIDS; although, that risk is negated if the patient is also taking low dose aspirin.

Typical symptoms of peptic ulcer disease include episodic gnawing or burning epigastric pain; pain occurring two to five hours after meals or on an empty stomach; and nocturnal pain relieved by food intake, antacids, or antisecretory agents. A history of intermittent epigastric pain, relief of pain after food intake, and nighttime awakening because of pain are the most specific findings for peptic ulcer and help rule in the diagnosis. Less common features include indigestion, vomiting, loss of appetite, intolerance of fatty foods and heartburn. The physical examination is typically unreliable. The natural history and clinical presentation of peptic ulcer disease may differ in certain populations. Abdominal pain is absent in at least 30 percent of older patients with peptic ulcers. Postprandial epigastric pain is more likely to be relieved by food or antacids in patients with duodenal ulcers than in those with gastric ulcers. Weight loss precipitated by fear of food intake is characteristic of gastric ulcers. Silent ulcers and complications are more common in older patients and in patients taking NSAIDs. 18, 19

If the initial clinical presentation suggests the diagnosis of peptic ulcer disease, the patient should be evaluated for alarm symptoms, to include: evidence of bleeding, to include anemia, hematemesis, melena, and heme-positive stools, vomiting, anorexia, and weight loss. Patients older than 55 years and those with alarm symptoms, regardless of age, should be referred for prompt upper endoscopy. Esophagogastroduodenoscopy (EGD) is more sensitive and specific for peptic ulcer disease than upper gastrointestinal barium studies and allows biopsy of gastric lesions. Patients younger than

55 years with no alarm symptoms should be tested for *H. pylori* infection and advised to discontinue the use of NSAIDs, smoking, and alcohol. Presence of *H. pylori* can be confirmed with a urea breath test, serum enzyme-linked immunosorbent assay (ELISA), stool antigen test, endoscopic biopsy, culture or polymerase chain reaction. The urea breath test and stool antigen ELISA testing are the two most accurate tests (each with greater than 90% for both sensitivity and specificity) without being significantly invasive.<sup>1, 22</sup> Both tests can also be used to check for eradication. If test results are positive for *H. pylori*, the infection should be eradicated. After treatment for *H. pylori*, patients with persistent symptoms should be referred for endoscopy to rule out refractory ulcer and malignancy. Patients without alarm symptoms who respond well to therapy without relapse do not necessarily need endoscopy or radiographic studies.

Treatment of peptic ulcer disease should include eradication of *H. pylori* if the patient tests positive. Over the past 20 years, H. pylori eradication therapies have mainly consisted of antimicrobial agents combined with antisecretory drugs. Treatment of active ulcers always necessitates the use of a PPI as they have been shown to heal peptic ulcers more rapidly than H<sub>2</sub>-blockers or any other drug.<sup>21</sup> The most common first-line treatment is a triple therapy with a PPI twice daily plus clarithromycin 500 mg twice daily and either amoxicillin 1 g twice daily or metronidazole 500 mg twice daily for 7–14 days.<sup>22</sup> Another first-line treatment option includes sequential treatment consisting of five days of a PPI plus amoxicillin followed by five additional days of a PPI plus clarithromycin and tinidazole. However, this sequential treatment has not been validated in the US. 22, 24 Several other treatment options are considered second line, including non-bismuth-based quadruple therapy, bismuth-based quadruple therapy and levofloxacin triple therapy. <sup>1, 22</sup> Research has shown improved eradication rates and less diarrheal side effects if probiotics Saccharomyces boulardii (S. boulardii) and Lactobacillus strains are added to the current first line treatments. 1, 22 A 2015 review directly compared 34 different treatment combinations and determined that the standard 7 day triple therapy was the least effective in eradicating H. pylori. 25 The most effective treatments were found to be concomitant treatments (simultaneous PPI plus three antibiotics), 10 to 14 day probiotic supplemented triple therapy, 10 to 14 day levofloxacin-based triple therapy, 14 days of hybrid treatment (7 days simultaneous PPI plus amoxicillin, followed by 7 days simultaneous PPI with amoxicillin, clarithromycin and nitroimidazole) or 10 to 14 days of sequential treatment.<sup>25</sup> Increased resistance to antibiotics, especially clarithromycin needs to be considered in the selection of treatment. If there is 15 to 20% resistance rate to clarithromycin in the geographic region, a non-clarithromycin treatment should be used. 1, 22, 24 H. pylori eradication should be confirmed 4 weeks or more after treatment is completed in those with H. pyloriassociated ulceration.<sup>1, 22</sup> Patients who are smokers are two times more likely to fail *H. pylori* treatment.<sup>24</sup>

Eradicating *H. pylori* is often sufficient treatment for patients with small duodenal ulcers. Repeated EGD with biopsy is recommended to confirm healing of gastric ulcers and to rule out malignancy. A systematic review of randomized controlled trials showed that proton pump inhibitors healed duodenal ulcers in more than 95 percent of patients at four weeks and gastric ulcers in 80% to 90% of patients at eight weeks.<sup>23</sup> Therefore, there is little reason to prescribe proton pump inhibitors for longer than four weeks for duodenal ulcers unless the ulcers are large, fibrosed, or unresponsive to initial treatment. Maintenance therapy with H<sub>2</sub> blockers or proton pump inhibitors prevents recurrence in high-risk patients (e.g., those with a history of complications, frequent recurrences, ulcers testing negative for *H. pylori*, refractory giant ulcers, or severely fibrosed ulcers). However,

maintenance therapy is not generally recommended for patients in whom *H. pylori* has been eradicated and who are not taking NSAIDs long-term.

### IV. Aeromedical Concerns.

Sudden incapacitation due to perforation or hemorrhage is of primary concern. Ulcer pain may be distracting and interfere with performance during critical phases of flight. Chronic blood loss from PUD may lead to anemia, which can cause fatigue, weakness, lightheadedness and decreased Gz tolerance. Additionally, it could contribute to hypoxia and decreased tolerance of physical exertion.

| ICD 9 Codes for Peptic Ulcer Disease |  |
|--------------------------------------|--|
| 533                                  | Peptic Ulcer, Site Unspecified                                       |
| 533.0                                | Acute Peptic Ulcer of Unspecified Site with Hemorrhage               |
| 533.00                               | Acute Peptic Ulcer of Unspecified Site with Hemorrhage, without      |
|                                      | Mention of Obstruction   |
| 533.1                                | Acute Peptic Ulcer of Unspecified Site with Perforation              |
| 533.3                                | Acute peptic ulcer of unspecified site without mention of hemorrhage |
|                                      | and perforation  |
| 533.4                                | Acute Peptic Ulcer of Unspecified Site with Hemorrhage               |
| 533.9                                | Peptic Ulcer of Unspecified Site Unspecified as Acute or Chronic,    |
|                                      | Without Mention of Hemorrhage or Perforation                         |

| ICD 10 Codes for Peptic Ulcer Disease |   |
|---------------------------------------|---|
| K27.0                                 | Acute peptic ulcer, site unspecified, with hemorrhage                     |
| K27.1                                 | Acute peptic ulcer, site unspecified, with perforation                    |
| K27.2                                 | Acute peptic ulcer, site unspecified, with both hemorrhage and            |
|                                       | perforation   |
| K27.3                                 | Acute peptic ulcer, site unspecified, without hemorrhage or perforation   |
| K27.4                                 | Chronic or unspecified peptic ulcer, site unspecified, with hemorrhage    |
| K27.5                                 | Chronic or unspecified peptic ulcer, site unspecified, with perforation   |
| K27.6                                 | Chronic or unspecified peptic ulcer, site unspecified, with both          |
|                                       | hemorrhage and perforation  |
| K27.7                                 | Chronic peptic ulcer, site unspecified, without hemorrhage or perforation |
| K27.9                                 | Peptic ulcer, site unspecified, unspecified as acute or chronic, without  |
|                                       | hemorrhage or perforation   |
| Z87.11                                | Personal history of peptic ulcer  |

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# WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of Dec 2013

By: Dr Dan Van Syoc

Reviewed by: Dr. Edwin Palileo (ACS Cardiologist) and Lt Col Eddie Davenport (ACS Chief

Cardiologist) and AFMSA staff

# **CONDITION:**

Pericardial Disorders including Myopericarditis (Jan 2018)

### I. Waiver Consideration.

IAW MSD H19 "Pericarditis. Chronic constrictive pericarditis, unless successful surgery has been performed and return of normal hemodynamics objectively documented, and chronic serous pericarditis" is disqualifying for retention and will therefore require an MEB before waiver consideration. The same is true for H18 "Myocarditis and degeneration of the myocardium". Additionally, MSD H21 has implications for FC I/IA, II, III and SWA by making a history of pericarditis disqualifying. It states: "Pericarditis, myocarditis, or endocarditis, or history of these conditions." ACS review and evaluation is required in all flying classes.

**Table 1: Waiver potential for pericardial disorders.** 

| Flying          | Condition  | Waiver Potential | ACS               |
|-----------------|--|------------------|-------------------|
| Class (FC)      |  | Waiver Authority | Evaluation/Review |
| I/IA            | Uncomplicated idiopathic/viral pericarditis, off all medications and ≥6 months since episode                                     | Yes<br>AETC      | Yes               |
|                 | Complicated pericarditis including pericarditis with effusion and myopericarditis, off all medications and ≥1 year since episode | Maybe<br>AETC    | Yes               |
|                 | Other pericardial disorders  | Maybe<br>AETC    | Yes               |
| II/III          | Uncomplicated idiopathic/viral pericarditis*   | Yes<br>MAJCOM    | Yes               |
|                 | Complicated pericarditis including pericarditis with effusion and myopericarditis†   | Maybe<br>MAJCOM  | Yes               |
|                 | Other pericardial disorders  | Maybe<br>MAJCOM  | Yes               |
| GBO/ATC/<br>SWA | Uncomplicated idiopathic/viral pericarditis*   | N/A              | No                |
|                 | Complicated pericarditis including pericarditis with effusion and myopericarditis†   | Yes<br>MAJCOM    | No                |
|                 | Other pericardial disorders  | Yes<br>MAJCOM    | No                |

<sup>\*</sup> Waiver for pericarditis and the use of NSAID (total of <u>6-8 weeks</u> of treatment) may be submitted one month after complete resolution of symptoms.

AIMWITS search in Jan 2018 revealed 93 cases with the diagnosis of pericarditis. There were a total of 12 disqualifications. Breakdown of the cases was as follows: 5 FC I/IA cases (1 disqualified), 51 FC II cases (2 disqualified), 4 RPA pilot cases (1 disqualified), 32 FC III cases (7 disqualified), and 1 ATC/GBC case (1 disqualified). Only one of the disqualified cases was primarily due to issues with pericardial disease.

<sup>†</sup> Waiver may be submitted three months after complete resolution of clinical illness.

# II. Information Required for Waiver Submission.

Prior to waiver submission for uncomplicated pericarditis there is a minimum nonflying observation period of one month after symptom resolution (6 months for FC I/IA). The aviator may be on an approved NSAID at the time of waiver submission, in order to complete above recommended 6-8 weeks of anti-inflammatory therapy. For aviators with complicated pericardial disorders (e.g. pericarditis with effusion or myopericarditis), there is a minimum nonflying observation period of three months (12 months for FC I/IA). The minimum three month observation period should start at the resolution of the clinical illness (e.g. echo-proven resolution of associated effusions or wall-motion abnormalities).

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for pericardial disorders should include the following:

- A. Complete history and physical exam to include description of symptoms before and after the acute episode, medications, and activity level. Pertinent negatives should include absence of disorders known to affect the pericardium (e.g. uremia, tuberculosis, recent MI, prior trauma).
- B. Electrocardiogram (ECG).
- C. Chest x-ray report.
- D. Copy of all local echocardiogram reports. Send videotape/CD copy of the echocardiographic images to the ACS. (Notes 1 and 2)
- E. Copies of reports and tracings/images of any other cardiac tests performed locally for clinical assessment (e.g. treadmill, Holter monitor, cardiac cath, cardiac CT or MRI). If reports not attached in AIMWTS, send to the ACS. (Notes 1 and 2)
- F. Results of medical evaluation board (MEB) if required (worldwide duty evaluation for ARC members).
- G. Additional local cardiac testing is not routinely required but may be requested in individual cases.

The AMS for waiver renewal for pericardial disorders should include the following:

- A. Interval history since last waiver approval
- B. All applicable labs and imaging tests as in the initial aeromedical summary.
- C. Consultation from treating cardiologist or internist

Note 1: The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

To expedite the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

### III. Overview.

The pericardium is a fibrous structure surrounding the heart composed of visceral and parietal layers separated by a pericardial cavity, which normally contains up to 50 mil of serous fluid. Pericardial disorders include any abnormality involving the pericardium. Acute pericarditis most commonly arises either from idiopathic causes (80 to 90% of cases in the U.S.) or a precipitating viral illness such as an upper respiratory infection (URI). Acute disease is common and must be considered in the differential diagnosis of chest pain in adults. The incidence of acute pericarditis is unknown, but it does account for approximately five percent of patients presenting with nonischemic chest pain to emergency departments. Interestingly, patients with congenital or surgical absence of the pericardium show few, if any, clinical problems. Acute disease is common and must be

Other less frequent causes of acute pericarditis include other infectious etiologies (such as tuberculosis), cancer, rheumatic disease, metabolic conditions (hypothyroidism, uremia), drugrelated, radiation-induced and post acute myocardial infarction (MI). There is also an association of pericarditis with smallpox vaccination. As of March 23, a total of 10 cases of myocarditis and/or pericarditis have been identified among approximately 225,000 primary vaccines in the military smallpox vaccination program. All had onset of chest pain 6--12 days following vaccination and all had clinical, laboratory, electrocardiographic, and/or echocardiographic evidence of myocardial and/or pericardial inflammation. None of the cases was clinically severe, and all patients recovered fully and returned to active duty.<sup>8</sup> In another study there were a total of 70 cases out of 721,600 service members deployed to Iraq and Kuwait from 2004 to 2008 that had pericarditis and myopericarditis. 4/11 had pericarditis and 7/11 had myopericarditis 13-28 days after smallpox vaccination.<sup>9</sup>

Post-traumatic pericarditis may also occur, including post-surgical.<sup>10</sup> Most cases of idiopathic or viral-related acute pericarditis are self-limited disorders and resolve either spontaneously or with conservative treatment. Pericarditis may occasionally be complicated by the presence of a pericardial effusion or by pericardial thickening. Only rarely do acute pericarditis-associated effusions result in clinically significant situations such as pericardial tamponade. Inflammatory-associated pericardial thickening may rarely progress to constrictive pericarditis.<sup>7</sup>

Other conditions involving the pericardium are rarer. Myopericarditis is a condition in which the inflammation of the pericardium spreads to the underlying myocardium itself. This is marked by the presence of positive cardiac enzymes in routine blood work, and can be complicated by myocardial wall-motion abnormalities, although overall left ventricular systolic function is usually normal. Myopericarditis typically resolves with usual anti-inflammatory therapy. This should be differentiated from primary myocarditis without associated pericarditis, typically associated with either global hypokinesis and/or a reduction in overall left ventricular ejection fraction.<sup>2</sup> This usually portends a much poorer prognosis (see cardiomyopathy waiver guide). Additional unusual pericardial diseases include pericardial cysts and congenital absence of the pericardium.

Acute pericarditis is typically diagnosed by a triad of historical symptoms, clinical signs, and routine testing (e.g. ECG). The usual pain is a pleuritic-type pain which is often worse when lying supine and relieved by sitting upright. It may or may not have a respiratory component. The classic three-phase friction rub is highly specific, but sensitivity varies as the rub is variably present on physical examination. The typical ECG pattern of diffuse ST-segment elevation may or may not be

present.<sup>4, 11</sup> Most cases of acute pericarditis resolve after a few days to weeks of anti-inflammatory drug therapy such as aspirin and nonsteroidal anti-inflammatory drug (NSAID). Aspirin (2 to 4 grams), indomethacin (75 to 225 mg daily), and ibuprofen (1600 to 3200 mg daily) are prescribed most often, with ibuprofen preferred, since it has a lower incidence of adverse effects than the others.<sup>1</sup> Colchicine, alone or in combination with an NSAID, can be considered for patients with recurrent or continued symptoms beyond 14 days.<sup>12</sup>

Treatment should last at least 7-14 days. A full-dose NSAID should be maintained until normalization of the C-reactive protein (CRP) followed by gradual tapering of the drug for another 1-2 weeks to prevent early reoccurrence. Corticosteroids should not be used for initial treatment of pericarditis unless it is indicated for the underlying disease, the patient's condition has no response to NSAIDs or colchicine, or both agents are contraindicated. Steroids are not administered initially as their use is associated with an increased incidence of recurrent pericarditis. The most common cause of recurrent pericarditis and waiver denial is insufficient treatment duration.

The literature state that 15% to 30% of all cases of acute pericarditis will go on to recurrent disease. Recurrence of symptoms following an acute uncomplicated case of pericarditis are usually related to premature discontinuation of anti-inflammatory treatment. The underlying inflammatory process usually lasts 6-8 weeks, although symptoms typically resolve within just a few days of initiating anti-inflammatory treatment. The tendency to suspend treatment (often done after about two weeks if the patient is asymptomatic) with resolution of symptoms should therefore be avoided, and a 6-8 week course of treatment is recommended to avoid symptom recurrence. If recurrence does occur then NSAID and colchicine are the preferred treatment, with glucocorticoids reserved for treatment failure. Another encouraging fact is that the vast majority of patients with recurrent pericarditis have an excellent overall life prognosis with a very small incidence rate of cardiac tamponade and no reported cases of restrictive pericarditis. 15

# IV. Aeromedical Concerns.

Aeromedical concerns surrounding uncomplicated, acute pericarditis revolve around the potential for sudden complications, the ability to perform flight duties while the active inflammatory state is underway, recurrence of symptoms, and medical treatment. Arrhythmias are very rare occurrences in individuals with idiopathic or viral pericarditis, and as such the risk for sudden incapacitation is rare. <sup>16</sup> Treatment regimens for acute, uncomplicated pericarditis typically are limited to NSAIDs or glucocorticoids. NSAIDs (ibuprofen, aspirin and naproxen) are waiverable medications once symptoms have resolved. Glucocorticoids and colchicine are not waiverable, as side effects are not compatible with aircrew duties.

Aviators with a history of completely treated (6-8 weeks anti-inflammatory drug) idiopathic or viral pericarditis are very unlikely to develop recurrent episodes of pericarditis. In aviators with pericarditis complicated by significant pericardial effusion or myocardial inflammation, the aeromedical risks increase as effects on myocardial cellular function and overall hemodynamics are potentially increased. Return to full flying duties can occur when there is complete absence of active disease to include echocardiographic evidence of resolution of any effusion. <sup>17</sup> Complicated cardiac arrhythmias may occur, and regional wall motion abnormalities may compromise cardiac responses to physiologic stress. Furthermore, myopericarditis may require an extended period of treatment for complete resolution of any underlying wall motion abnormalities or resolution of associated pericardial effusion.

| ICD-9 codes for Pericarditis and Myopericarditis |                                    |  |
|--|------------------------------------|--|
| 420  | Acute pericarditis                 |  |
| 420.9  | Other and unspecified pericarditis |  |

| ICD-10 codes for Pericarditis and Myopericarditis |   |  |
|---|---|--|
| I30.9   | Acute pericarditis, unspecified               |  |
| I32   | Pericarditis in diseases classified elsewhere |  |

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## WAIVER GUIDE

Updated: Feb 2017

Supersedes Waiver Guide of Jun 2013

By: Lt Col Robert McCoy (RAM 18) and Dr Dan Van Syoc

Reviewed by ACS Neuropsychiatry staff

# **CONDITION:**

Personality Disorders (Feb 2017)

# I. Waiver Consideration.

A personality disorder that is severe enough to repeatedly manifest itself by significant interference with safety of flight, crew coordination, or mission completion is disqualifying for all flying classes and special duties positions. In addition, unsatisfactory duty performance due to personality disorder may cause the member to be technically unsuitable as opposed to unfit and subject to administrative separation. If the member has personality traits but does not meet the criteria for personality disorder, he or she still may be deemed ARMA Unsatisfactory. It is strongly recommended that all cases being considered for a waiver be reviewed by the ACS.

Table 1: Waiver potential for Personality Disorders<sup>1</sup>

| Flying Class (FC)     | Waiver Potential<br>Waiver Authority | ACS Review/Evaluation     |
|-----------------------|--------------------------------------|---------------------------|
| I/IA                  | No<br>AETC                           | Only if requested by AETC |
| II/III<br>ATC/GBO/SWA | Yes <sup>2,3</sup><br>MAJCOM         | Yes                       |

<sup>1</sup> All cases considered for waiver must be considered psychologically stable and manifestations no longer interfering with duty.

AIMWTS review in Nov 2016 produced a total of 121 cases with the diagnosis of personality disorder. Of this total, 5 were for FC I/IA, 19 were for FC II, 55 were for FC III, 35 were for ATC/GBC, 7 were for MOD. All but 14 of the total of 121 cases resulted in a disqualification; 4 approved waivers for FC II, 8 approved waivers for FC III, and 1 approved waiver for ATC/GBC. The vast majority of the cases had at least one other psychiatric diagnosis in addition to the diagnosis of personality disorder.

# II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

The Medical Standards Directory (MSD) and the Aeromedical Consultation Service (ACS) Waiver Guide addresses waiver evaluations

Step 1 - Is the aviator ready for waiver submission?

<sup>2</sup> Waiver not recommended for any initial flying class for individuals with a history of personality disorder.

<sup>3</sup> No indefinite waivers.

|                | Waiver is submitted when 1) the member is asymptomatic and 2) medications/psychotherapy treatment have been completed, as applicable to diagnostic category, for the specified time-frame below (Note: psychotherapy "booster sessions", and sometimes SSRIs, are permissible and often advisable after initial symptom resolution):  1 Year—Psychotic Disorders & Somatoform Disorders |
|----------------|---|
|                | 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior  |
|                | Discretion of Flight Surgeon—Adjustment Disorders & Z-Codes requiring waiver  |
|                | For Traumatic Brain Injury cases, please refer to TBI Waiver Guide  |
|                | For aviators with any other psychiatric disorders, please refer to MSD and ACS Waiver Guide   |
|                | To be considered for an aeromedical waiver, any disqualifying condition must meet the following criteria per MSD:   |
|                | Not pose a risk of sudden incapacitation  |
|                | Pose minimal potential for subtle performance decrement, particularly with regard to the  |
|                | higher senses  Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment   |
|                | If the possibility of progression or recurrence exists, the first symptoms or signs must be   |
| Г              | easily detectable and not pose a risk to the individual or the safety of others  Cannot require exotic tests, regular invasive procedures, or frequent absences to monitor  |
| L              | for stability or progression  |
|                | Must be compatible with the performance of sustained flying operations  |
| Ment<br>Instru | 2 - Before beginning the Aeromedical Summary (AMS), Flight Surgeon must obtain al Health consultation and ensure it contains items specified below: actions for the Mental Health Provider nental health evaluation must include a comprehensive written report addressing:  Consultation must address each criteria in Step 1B   |
|                | Clinical mental health history (description of symptoms, treatment modality, frequency and  |
| L              | compliance with treatment, relevant personal and family history, and perceived impact on occupational duties)   |
|                | Medication history (dates of initial prescription and termination, reason for termination, dosage,  |
|                | compliance, response, clinical course since termination)  Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)  ** for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results**   |
|                | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental illness)   |
|                | Current and past aviation related duties and any history of current and past occupational performance difficulties (to include perceived impact of mental health condition on performance   |
|                | of duties)  Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)   |
|                | Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact  |

|      |                  | ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended neuropsychological tests.  Current mental status   |
|------|------------------|---|
|      |                  | Diagnosis   |
|      |                  | Motivation to fly or engage in special duty operations (past and current)   |
|      |                  | Recommendation for future psychological and medical treatment   |
|      |                  | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
|      |                  | Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand for shipment to ACS Neuropsychiatry Branch   |
| Step | 3 -              | Items for the Flight Surgeon to include in the AMS:  AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safety  |
|      |                  | Summarize Mental Health history and focus on occupational impact  ** If 2 or more months have passed since the comprehensive evaluation/report was completed, the flight surgeon should address how the member has done since and consult with the mental health provider if the member has been seen at mental health since the evaluation** |
|      |                  | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)   |
|      |                  | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)   |
|      |                  | ** for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results**  Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if possible - please address current state of any triggers for the mental illness)  |
|      |                  | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)   |
|      |                  | Current mental status   |
|      |                  | Diagnosis   |
|      |                  | Motivation to fly (past and current)  |
|      |                  | Recommendation for future psychological and medical treatment   |
|      |                  | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
| Step |                  | Items to complete the waiver package:   |
|      |                  | tter of support from command  |
|      |                  | mprehensive mental health written report  |
| Ш    | Co               | nfirm mental health has made copies of chart(s) and testing. When requested send to:  |
|      | c/o<br>25:<br>Wi | CS Aerospace Medicine Branch, USAFSAM/FECA Neuropsychiatry Branch 10 Fifth Street Bldg 840 right Patterson AFB, OH 45433-7913   |
| Plea |                  | x: (937) 904-6296 DSN: 674-9296 eel free to contact the ACS Neuropsychiatry Branch with questions:  |
|      |                  | Valter Croft: DSN 798-2778 or Mr. John Heaton: 798-2766   |

The AMS should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> for personality disorders should include the following:

A. History – symptoms, good time-line of events; how symptoms affect job, home life, finances, legal issues and relationships. Discuss all other psychiatric conditions. Include drinking and drug use history, if applicable.

- B. List and fully discuss all clinical diagnoses requiring a waiver.
- C. Treatment medications and therapy used for all psychiatric conditions.
- D. Psychiatry/psychology consultation report(s).
- E. Report of all psychological testing, if performed.
- F. Letters of support from squadron commander
- G. Medical evaluation board results, if applicable.

The AMS for <u>waiver renewal</u> for personality disorders should include the following:

- A. History interim history since last waiver submission to include reports of any legal or job-related problems.
- B. Treatment current therapy for the condition, if any.
- C. Psychiatry/psychology consultation report(s).

## III. Overview.

Personality traits are enduring patterns of perceiving, relating to, and thinking about the environment and are exhibited in a wide range of contexts. Only when these traits are inflexible, maladaptive or cause significant functional impairment, is the individual identified as having a personality disorder. The essential feature of a personality disorder is an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture. There are six criteria that must be met. The problematic pattern of inner experience and behavior is manifested in two (or more) of the following areas: Cognition, affectivity, interpersonal functioning, or impulse control (Criterion A). This enduring pattern is inflexible and pervasive across a broad range of personal and social situations (Criterion B) and leads to clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The pattern is stable and of long duration, and its onset can be traced back to at least adolescence or early adulthood (Criterion D). The pattern is not better explained as a manifestation or consequence of another mental disorder (Criterion E) and is not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication, exposure to a toxin) or another medical condition (e.g., head trauma) (Criterion F). By definition, the symptoms of a personality disorder cannot be caused by another psychiatric disorder as diagnosed in DSM-5.<sup>2</sup> But it is not uncommon for patients with a personality disorder to have another psychiatric conditions, and it is often the other condition that brings the case to the attention of mental health professionals and drives a psychiatric evaluation.

Personality disorders are common in US society. The prevalence is reported to be 15% in the general population and account for 45.5% of patients presenting for outpatient psychiatric care.<sup>3</sup> Rates increase dramatically in select populations. For example, it is estimated that more than 28% of patients with alcohol disorders and 47% of patients with drug use disorders also have a personality disorder.<sup>4</sup> Although these conditions are chronic, they often will improve over time.

The prognosis for many with personality disorders is better than many other serious mental health conditions.<sup>5</sup> This improvement in personality psychopathology may be associated with a real reduction in ongoing personal and social burdens according to a 2008 review of four large-scale studies.<sup>7</sup> Conversely, findings by Skodol et al support the growing clinical literature on the adverse prognostic effects of personality disorders on the course of major depressive disorder.<sup>7</sup> Current classifications of personality disorders in DSM-5 have no measure of severity.

Personality disorders are divided into three major areas called clusters. Cluster A is identified as odd or eccentric and include the subtypes of schizoid, schizotypal, and paranoid personality disorders. Cluster B is identified as dramatic, emotional or erratic and includes antisocial, borderline, histrionic, and narcissistic personality disorders. Cluster C is the more prevalent of the personality disorders and is identified as anxious or fearful. It includes avoidant, dependent, and obsessive-compulsive personality disorders.<sup>2</sup> An individual may have traits from different clusters and may meet criteria from more than one personality disorder.

Management is directed primarily toward the more predominant symptom characteristics. Initially, efforts are focused on maintaining and supporting the patient-physician relationship and establishing a working alliance. The treating physician needs to have a good understanding of the personality characteristics of these patients and work to adapt his or her style in order to optimize communication and the ultimate clinical outcome. Psychotropic medications are not a front-line approach to the care of most of patients. If a particular case lends itself to treatment with medications, it should not be attempted by a non-mental health professional.

# IV. Aeromedical Concerns.

For all flying classes the question of "suitability" is important. Personality disorders and traits may impact performance of military duty, including aviation duty and flight safety, because of associated social, occupational, administrative, and legal ramifications. As a general rule, successful treatment requires long-term, time intensive psychotherapy that can render the service member unavailable for full duty performance for a prolonged period of time. When a personality disorder diagnosis is confirmed by mental health consultation, administrative separation due to psychological unsuitability for military service is often pursued. This administrative action requires evidence of negative impact on duty performance due to the disorder, in addition to the diagnosis of the disorder itself. Typically, other potentially medically disqualifying disorders are considered and ruled out before taking this action.

Unfortunately, many persons with personality disorders spend a long time between initial referral for evaluation and final diagnosis and disposition decision making. Care is needed to avoid hasty over-diagnosis of personality disorders in personnel with idiosyncratic personality traits. Thus, in questions of possible administrative separation action by command, early consultation with a mental health provider should be considered. The flight surgeon and mental health provider may assist the commander in the decision-making process through explanation of personality disorder manifestations and discussion of the associated prognosis.

People with personality disorders often have difficulty working closely with others under stressful conditions, in adhering to discipline, and in responding appropriately to authority, all of which can threaten flight safety and mission completion. They can be rigid, unwilling to compromise and

often express anger explosively or indirectly, thereby creating interpersonal tension that can be disruptive to the good order and discipline of a unit. Behavior rooted in personality disorders (e.g., temper outbursts, unreliability, chronic non-adherence to unit or flight discipline, and passive-aggressive behavior) may threaten flight safety and can lead to command-directed mental health evaluations. It is appropriate to DNIF such a flyer pending mental health evaluation. It is also paramount that supervisors document all negative behavior as the diagnosis is made by examining behavior patterns over time. These disorders are considered to be inherent to the individual and a permanent part of their personality.

| ICD-9 codes for Personality Disorder <sup>14</sup> |   |  |
|--|---|--|
| 310.1  | Personality Change Due to Another Medical |  |
|  | Condition                                 |  |
| 301.22   | Schizotypal Personality Disorder          |  |
| 301.0  | Paranoid Personality Disorder             |  |
| 301.20   | Schizoid Personality Disorder             |  |
| 301.7  | Antisocial Personality Disorder           |  |
| 301.83   | Borderline Personality Disorder           |  |
| 301.54   | Histrionic Personality Disorder           |  |
| 301.4  | Obsessive-Compulsive Personality Disorder |  |
| 301.82   | Avoidant Personality Disorder             |  |
| 301.6  | Dependent Personality Disorder            |  |
| 301.81   | Narcissistic Personality Disorder         |  |
| 301.89   | Other Specified Personality Disorder      |  |
| 301.9  | Unspecified Personality Disorder          |  |

| ICD-10 codes for Personality Disorder <sup>14</sup> |   |  |
|---|---|--|
| F07.0   | Personality Change Due to Another Medical |  |
|   | Condition                                 |  |
| F21   | Schizotypal Personality Disorder          |  |
| F60.0   | Paranoid Personality Disorder             |  |
| F60.1   | Schizoid Personality Disorder             |  |
| F60.2   | Antisocial Personality Disorder           |  |
| F60.3   | Borderline Personality Disorder           |  |
| F60.4   | Histrionic Personality Disorder           |  |
| F60.5   | Obsessive-Compulsive Personality Disorder |  |
| F60.6   | Avoidant Personality Disorder             |  |
| F60.7   | Dependent Personality Disorder            |  |
| F60.81  | Narcissistic Personality Disorder         |  |
| F60.89  | Other Specified Personality Disorder      |  |
| F60.9   | Unspecified Personality Disorder          |  |

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# WAIVER GUIDE

Updated: Aug 2016

Supersedes Waiver Guide of Mar 2012

By: Lt Col Bryant Martin (RAM 2017) and Dr Dan Van Syoc

Reviewed by Lt Col Irene Folaron, AF/SG consultant for Endocrinology

# **CONDITION:**

**Pituitary Tumors (Aug 2016)** 

# I. Waiver Consideration.

All pituitary tumors, whether benign or malignant, are disqualifying for all flying classes, ATC, GBO and SWA duties, as well as retention. The severity of the condition, the medications required to control the condition and/or complications/results of surgery impact the waiver decision-making process.

Table 1. Waiver potential for pituitary tumors.

| Flying                | Condition   | Waiver Potential | ACS               |
|-----------------------|---|------------------|-------------------|
| Class                 |   | Waiver Authority | review/evaluation |
| I/IA                  | Incidental microadenomas, non-  | Yes              | Yes               |
|                       | functional, unchanged for 2 years   | AETC             |                   |
|                       | Nonfunctioning micro or macroadenomas treated with surgery and requiring no pharmacotherapy | Maybe<br>AETC    | Yes               |
|                       | Secreting microadenoma or macroadenoma treated with or without pharmacotherapy or           | No<br>AETC       | No                |
|                       | treated with surgery and requiring pharmacotherapy  Pituitary carcinoma                     | No<br>AETC       | No                |
| II//III<br>ATC<br>GBO | Microadenomas, non-functional   | Yes<br>MAJCOM    | Yes               |
| SWA                   | Secreting prolactinoma, asymptomatic requiring no pharmacotherapy                           | Yes*<br>AFMRA    | Yes               |
|                       | Micro or macroadenomas treated with surgery, in remission and                               | Maybe*<br>AFMRA  | Yes               |
|                       | micro or macroadenomas treated with or without surgery and                                  | No<br>AFMRA      | No†               |
|                       | requiring pharmacotherapy  Pituitary carcinoma  | No<br>AFMRA      | No                |

<sup>\*</sup> Waiver for untrained FC II and III is unlikely.

AIMWTS search in Jun 2016 revealed a total of 58 individuals with a diagnosis of a pituitary tumor. There were a total of 11 disqualifications. Breakdown of the cases was as follows: 4 FC I/IA cases (4 disqualifications), 29 FC II cases (1 disqualification), 19 FC III cases (4 disqualifications), 4 ATC/GBC cases (2 disqualifications), and 2 MOD cases (0 disqualifications. All 11 disqualified cases were related to the pituitary diagnosis.

<sup>†</sup> If pharmacotherapy is stopped after an interval (12-24 months) and remission is maintained for six months, waiver will be considered after ACS review.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> should include the following:

- A. List and fully discuss <u>all</u> clinical diagnoses requiring a waiver.
- B. Thorough history and physical to identify possible endocrinologic, neurologic, or ophthalmologic clinical findings with directed evaluation based on findings.
- C. MRI of pituitary or CT if unable to perform MRI.
- D. Serum PRL level for all pituitary tumors.
- E. Endocrinology consult to include need for further hormonal evaluation and management.
- F. Neurosurgery consult for evaluation for surgery on any pituitary tumor other than prolactinoma or incidentaloma, or any pituitary tumor with suspected mass effect.
- G. Baseline formal visual field testing (Humphrey visual field 30-2), acuity, and dilated funduscopic exam. If surgery is performed, then repeat testing afterwards.
- H. Echocardiogram in GH secreting pituitary adenoma.
- I. MEB results.

Note: If steroids are temporarily required after treatment of ACTH pituitary adenoma, see waiver guide on systemic glucocorticoid (steroid) treatment.

The AMS for waiver renewal for pituitary tumor should include the following:

- A. History brief summary of initial work-up, interval signs or symptoms including pertinent negatives.
- B. Physical complete with focus on previous findings.
- C. MRI/CT of pituitary annually for first two years, then every two years if stable.
- D. Endocrinology consult.
- E. Formal visual field testing and acuity testing annually for macroadenomas (not needed if a macroprolactinoma and has responded to therapy), history of surgery/radiation therapy, or increase in tumor size, and more frequently as indicated for any visual complaints.

# III. Overview.

Pituitary tumors represent 15% of all primary intracranial tumors and are derived from hormone-secreting adenohypophyseal cells.<sup>1</sup> Primary pituitary tumors are either adenomas or carcinomas. Fortunately, pituitary carcinomas are exceedingly rare with an incidence of less than 0.5% of symptomatic lesions.<sup>2, 3</sup> Pituitary adenomas are benign anterior pituitary lobe neoplasms that comprise over 90% of pituitary tumors. The annual incidence of pituitary adenoma traditionally has been reported as approximately 1 in 10,000.<sup>4</sup> However, the prevalence of pituitary adenomas was 16.7% on a recent meta-analysis of autopsy (14.4%) and radiological (22.5%) data.<sup>5</sup> A more recent study of a population in the UK showed a prevalence of 77.6 per 100,000.<sup>6,7</sup>

Pituitary adenomas are the most common cause of sellar masses from the third decade on, accounting for up to 10 percent of all intracranial neoplasms.<sup>8</sup> They are classified by their size and

hormone secreted. Microadenomas are less than 10 mm and macroadenomas are 10 mm or greater. The five types based on hormone secretion are lactotroph (prolactin [PRL]), gonadotroph (nonfunctioning), somatotroph (growth hormone [GH]), corticotroph (adrenocorticotropic hormone [ACTH]), and thyrotroph (thyroid-stimulating hormone [TSH]). Some pituitary adenomas have multiple hormones released, such as PRL/GH and LH/FSH/TSH. Approximate frequency of adenomas are PRL (35%), nonfunctioning (30%), GH (20%), PRL/GH (7%), ACTH (7%), and LH/FSH/TSH (1%), and TSH (<1%). 11, 12

Prolactinoma (lactotroph adenoma), the most common category causes hyperprolactinemia. Common signs and symptoms are amenorrhea/oligomenorrhea with anovulation, galactorrhea, and infertility in females and impotence, infertility, and diminished libido in men. 13, 14, 15 Gonadotrophs, nonfunctioning adenomas, are the most common macroadenomas due to the late presentation of symptoms secondary to local mass effects. 16 Typical findings would include headache, visual field defects (classically bitemporal hemianopsia from optic chiasm compression), diplopia, hypopituitarism, and hypogonadism.<sup>4</sup> Although all types of adenomas can present with mass effect findings, primary secretory hormone types usually will present with their hormonal based symptoms earlier. Somatotroph produces hypersecretion of GH and the liver secretes insulin-like growth factor-1 (IGF-1) in response to the GH, which leads to acromegaly in adults. Physical findings include coarse facial features, acral enlargement, prognathism, hirsutism, and osteoarthritis. 17 Corticotrophs produce ACTH, which act on the adrenal gland and lead to hypercortisolemia, also known as Cushing's disease. Most are diagnosed as microadenomas secondary to relatively early clinical findings of truncal obesity, facial plethora, acne, hirsutism, striae, hypertension, osteopenia and muscle weakness.<sup>4</sup> Thyrotrophs produce TSH, which act on the thyroid gland and cause hyperthyroidism. The clinical findings are goiter, visual impairment, and thyrotoxicosis. 12

The evaluation of pituitary adenomas involves endocrinological, neurological, ophthalmological, and radiological considerations. The evaluation is driven by clinical findings discussed previously and appropriate screening tests looking for hyposecretion or hypersecretion of related hormones to support clinical findings. These screening tests are summarized in Table 1.<sup>1, 12</sup>

Table 2. Screening tests for functional pituitary adenomas.<sup>31</sup>

| Condition  | Test  | Comments  |
|--|---|---|
| Acromegaly   | IGF-I.  | Interpret IGF-I relative to age- and gender-matched controls.   |
|  |   | Exclude medications. Magnetic resonance imaging (MRI) of the sella should be ordered if PRL levels elevated.                                |
|  | 24-hr urinary free cortisol.  | Ensure urine collection is total and accurate.  |
| Cushing's disease  | Dexamethasone (1 mg) at 11 pm and fasting plasma cortisol measured at 8 am. | Normal subjects suppress to <1.8 $\mu$ g/dL (sensitivity of 95%). Other cut-offs such as < 3-5ug/dL are used at the expense of sensitivity. |
|  | Late-night Salivary cortisol test. 18                                       | Normal subjects should be < 145 ng/dL or reference range  |
| Hyperthyroidism   Serum TSH and free thyroxine (T4) levels.   Normal to elevated TSH and elevated followed levels. |   | Normal to elevated TSH and elevated free T4 levels.   |

For radiological evaluation of the pituitary, high resolution T-1 weighted MRI in coronal and sagittal planes with and without gadolinium is the gold standard. However, the increasing resolution and availability of MRI and CT in brain imaging has spawned more incidental findings of pituitary tumors (incidentalomas) with these asymptomatic lesions present in 10% of the general population. The majority of these lesions are microadenoma; in two years of follow-up only two percent showed enlargement as compared to about a third of macroadenomas. In asymptomatic patients, a single assay for PRL is usually sufficient for hormonal evaluation of an incidentally found microadenoma, although the Endocrine Society suggests an assessment for hypersecretion of prolactin, GH, and ACTH as part of the initial workup. For microadenomas (less than 1 cm), a sella MRI should be repeated annually for up to 3 years, then less frequently thereafter if there has been no change in the lesion size. The significant of the initial workup is the region of the lesion size.

The primary goals of treatment are to normalize excess pituitary secretion, alleviate signs and symptoms, shrink or eliminate compression of vital structures, and preserve or restore normal pituitary function.<sup>13</sup> These goals are approached by medical therapy, surgery, irradiation, or a combination.

Prolactinomas, the most common of pituitary adenomas, are primarily treated with pharmacotherapy or observation. Observation is a viable option in asymptomatic microprolactinomas because 95% of tumors do not enlarge in four to six years of observation. Dopamine agonists such as bromocriptine (Parlodel®) and cabergoline (Dostinex®) are the mainstay of therapy. Bromocriptine is taken two to three times daily compared with the longer acting cabergoline, which is taken twice weekly. Both drugs are effective in decreasing PRL levels and tumor size reduction in over 90% of patients, with cabergoline demonstrating slightly greater efficacy. Withdrawal of dopamine agonists after 1-3 years have shown no recurrence of hyperprolactinemia in 25.8 – 69%; the ideal candidate is one with normal prolactin concentrations while on dopamine agonists and small or no visible tumor on MRI prior to discontinuation of the

dopamine agonist.<sup>22</sup> The principal side effects of dopamine agonists are nausea, vomiting, postural hypotension, mental fogginess, and infrequently nasal stuffiness, psychosis, depression, hallucinations, nightmares, insomnia, vertigo, and Raynaud's phenomenon.<sup>13, 22</sup> Many of the adverse symptoms can be managed clinically with reduction in dose.<sup>13, 22, 25</sup> Nonetheless, the adverse effects are highly significant from an aeromedical standpoint.

If pharmacotherapy does not control the symptoms of hyperprolactinemia, or shrink a prolactinoma that is exerting mass effect, then surgery is an option.<sup>26</sup> For all other pituitary tumors, surgery is the primary treatment modality.<sup>1</sup> Endoscopic pituitary surgery has emerged as the first-line surgical treatment of choice with the exception of prolactinomas.<sup>27</sup> Postoperative remission for pituitary adenomas range from 73-96% (lowest GH secreting, highest nonfunctional), recurrence over 10 years is 8-13%. In adenomas which have resulted in visual deficits, visual recovery rates range from 88-92%.<sup>4</sup> All individuals should have extensive neuro-ophthalmological examination to include visual fields and acuity as well as fundoscopic exam prior to and following surgery.

For nonprolactinomas, other pharmacologic agents may be used as adjuncts to surgery. Acromegaly is treated primarily with somatostatin analogs, such as octreotide (Sandostatin®) and lanreotide (Somatuline®). Somatostatin analogs have been shown to shrink GH-secreting adenomas by 19.4%. Somatostatin analogs are limited by side effects to include gallstones and biliary sludging, nausea, cramps, and steatorrhea. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Ketoconazole, which inhibits steroid biosynthesis at the adrenal gland, is used as adjuvant therapy in Cushing's disease, both prior to surgery and afterwards if resection fails to result in complete control. Liver enzyme elevations, gynecomastia in men, gastrointestinal upset, and edema are common side effects and ketoconazole is notorious for a wide range of serious drug interactions. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have shown good efficacy in TSH-secreting adenomas as well. Somatostatin analogs have sh

Pituitary radiation is indicated for surgical failure, residual mass effects, persistent hormone hypersecretion, or when surgery is contraindicated. Concerns with pituitary radiation are hypopituitarism (80% within 10 years), other primary brain tumors (< 5% gliomas/meningiomas), optic nerve damage (2%), and brain necrosis (potential cognitive dysfunction, especially memory loss). The introduction of more precise techniques, such as gamma-knife and linear accelerator, should decrease the amount of radiation and collateral impact mentioned previously. Follow up after surgery or radiation should include serial clinical, endocrinologic, ophthalmologic, and radiologic studies. A postoperative MRI should be performed within three months of surgery or treatment and annual evaluations for tumor recurrence or residual. A summary of the management and control of pituitary adenomas is summarized in Table 2. 13

Table 3. Management and control of hormone hypersecretion in pituitary adenomas.

| able 3. Wanagement and control of normone hypersecretion in pituitary adenomas. |  |  |  |   |  |
|---|--|--|--|---|--|
| Approach  | Prolactin-<br>Secreting<br>Tumors  | Growth Hormone- Secreting Tumors   | ACTH-<br>Secreting<br>Tumors   | TSH-<br>Secreting<br>Tumors                   | Nonfunctioning<br>Tumors                             |
| Primary<br>Approach   | DA:<br>microadenomas,<br>80% to 90%<br>response;<br>macroadenomas,<br>60% to 75%<br>response | Surgery:<br>microadenomas,<br>70% response;<br>macroadenomas,<br>50% response  | Surgery: microadenoma, 80% to 90% response; macroadenoma, 50% response | Surgery plus irradiation, 67% response        | Surgery:<br>improved<br>vision, 70%<br>response      |
| Secondary<br>Approach   | Surgery:<br>microadenomas,<br>55% response;<br>macroadenomas,<br>20% response                | Somatostatin<br>analogues, 60%<br>response; DA,<br>20% response;<br>irradiation, 50%<br>response (by 12<br>years)        | Irradiation plus<br>cortisol-<br>decreasing<br>drugs                   | Somatostatin<br>analogues,<br>75%<br>response | Irradiation  |
| Novel<br>medical<br>developments  | Depot long-<br>acting DA,<br>somatostatin<br>receptor<br>subtype-selective<br>analogues      | Long-acting somatostatins, somatostatin receptor subtype-selective analogues, growth hormone receptor or GHRH antagonist |  | Long-acting somatostatins                     | Gonadotropin-<br>releasing<br>hormone<br>antagonists |

ACTH – adrenocorticotropin hormone; DA – dopamine agonists; GHRH – growth hormone releasing hormone; TSH – thyroid-stimulating hormone; Response refers to normalization of hormone secretion or ablation of tumor mass

Long-term monitoring of these conditions is variable, related to the condition and the response of the condition to the medical treatment. In general, normalization of abnormal hormone secretion and prevention of clinical signs and symptoms is the goal. The monitoring of serum markers will be more frequent (every 4-6 weeks) initially until stability is achieved. Pituitary MRI should show stability for 1-2 years before the interval is extended.<sup>27</sup>

# IV. Aeromedical Concerns.

Pituitary apoplexy, a hemorrhage into the pituitary tumor, is likely to cause sudden incapacitation but is exceedingly rare.<sup>32</sup> The main concerns for the pituitary tumors are related to hormone hypersecretion, the medications used to treat them, and mass-effect. For prolactinomas the primary concern is the side effects of the centrally-acting dopamine agonists used to treat some of these tumors, such as bromocriptine and cabergoline. These agents commonly cause headache and dizziness, as well as hypotension, syncope, drowsiness, fatigue, and vertigo. Dopamine agonists are

frequently sedating, and reports of sleep attacks, which initially were described in Parkinson's patients, have now been described in other conditions with these agents.<sup>34</sup> (Whether these drugs are excitatory or sedating is dependent on dose, time, and individual variance.) Psychosis, predominantly mania, occurs at unpredictable intervals; in one study, the average delay was 13.5 months (range 4-52 months) after inception of therapy.<sup>11</sup> Given the role of dopamine antagonism in the mechanism of action of antipsychotic drugs, the occasional occurrence of psychosis with dopamine agonism is not surprising. In addition, therapy with bromocriptine and cabergoline has been clearly associated with impulse control disorders, such as pathologic gambling, hypersexuality, and other behaviors.<sup>34, 35</sup>

These medications are not compatible with flying. GH-secreting adenomas, which cause acromegaly, are primarily treated with surgery, but somatostatin analogs are used for tumor shrinkage and suppression of GH prior to surgery. Common somatostatin analogs are octreotide and lanreotide and may be used continuously if individual is not a surgical candidate. These agents have common side effects to include biliary dysfunction, hypo/hyperglycemia, hypothyroidism and arrhythmias. The drug preparation requires refrigeration for storage since it is stable for only two weeks at 25°C. These considerations are clearly not compatible with either the flying or the deployed environment. Cushing's disease usually presents with hypersecretion symptoms that are adverse for flying such as hypertension, truncal obesity, hyperglycemia, and bruising.<sup>4</sup> Surgery is the preferred method of treatment secondary to poor medical response to treatment. These patients typically have a fair response to surgery, but need steroid replacement for up to 12 months after surgery.<sup>4</sup> Persistent steroid use and high recurrence rates after 5 years make this condition incompatible with aviation. TSH-secreting adenomas are more aggressive and cause all the side effects of hyperthyroidism with visual impairment and goiter. Pituitary carcinomas are extremely aggressive and have very poor prognosis.<sup>3, 30</sup>

The mass-effect seen with macroadenomas is another concern. Common symptoms related to this include headache and panhypopituitarism. With only a 1 cm gap between the pituitary and the optic chiasm, visual complications are common, and a complete visual workup needs to be done to evaluate for visual defects from compression of the chiasm or diplopia from oculomotor nerve impingement. Neuro-ophthalmologic finding could clearly impact individual performance and mission accomplishment. Except for prolactinomas, surgery is indicated when mass effect is present. If the prolactinoma doesn't respond to therapy, surgery may be indicated if the mass effect is clinically significant (i.e. mass effect on the optic chiasm causing bitemporal hemianopsia). As above, surgery has good remission rates and 10-year recurrence rates around 1% per year. Potential complications of surgery include CSF leak, transient diabetes insipidus, and inappropriate ADH secretion. Adjuvant radiotherapy or radiosurgery results in good control, but high rates of subsequent hypopituitarism. This may lead to issues with hormone replacement in the future.

| ICD-9 | ICD-9 codes for pituitary tumors   |  |
|-------|--|--|
| 194.3 | Malignant neoplasm in pituitary gland  |  |
| 227.3 | Benign neoplasm of pituitary gland craniopharyngeal duct (pouch)             |  |
| 242.8 | Thyrotoxicosis (overproduction of TSH)                                       |  |
| 253.0 | Acromegaly and gigantism (overproduction of growth hormone)                  |  |
| 253.1 | Other and unspecified anterior pituitary hyperfunction (except ACTH and TSH) |  |
| 255.0 | Cushing syndrome (overproduction of ACTH)                                    |  |

| ICD-10 codes for pituitary tumors |  |  |
|-----------------------------------|--|--|
| C75.1                             | Malignant neoplasm of pituitary gland  |  |
| D35.2                             | Benign neoplasm of pituitary gland     |  |
| E23.6                             | Other disorders of the pituitary gland |  |
| E22.0                             | Acromegaly and pituitary gigantism     |  |
| E22.8                             | Other hyperfunction of pituitary gland |  |
| E24.0                             | Pituitary-dependent Cushing's syndrome |  |

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#### WAIVER GUIDE

Updated: March 2020

Supersedes waiver guide of Aug 2016

By: Dr. Christopher Keirns and Dr. Dan Van Syoc

Reviewed by Lt Col Dara Regn, Chief, ACS Pulmonary and Sleep Medicine

# **CONDITION:**

Pneumothorax (Mar 2020)

# I. Waiver Considerations.

As of the July 2016 MSD, Air Force policy regarding spontaneous pneumothoraces has been significantly revised effectively making spontaneous pneumothorax disqualifying for FCI/IA/FCIII/SWA/OSF aviation duties. This new guidance applies to all initial flying class exams regardless of the date of prior pneumothorax as well as fully trained FCII/FCIII/SWA/OSF aviators experiencing a primary pneumothorax after the date of this publication. A single episode of spontaneous pneumothorax in a fully trained aviator prior to publication of this new MSD guidance would not require a waiver as long as results of PA inspiratory and expiratory chest radiographs and CT chest imaging are clearly documented in the medical record and show full expansion of the lung with no demonstrable pathology which would predispose to recurrence. If a fully trained FCII/FCIII/SWA/OSF aviator were to experience a recurrent pneumothorax, they would then require a waiver. Pneumothorax is not disqualifying for ATC or GBO personnel.

In summary, aeromedical waiver for spontaneous pneumothoraces may be considered only if PA inspiratory and expiratory chest radiograph and CT chest scan show full expansion of the lung and no demonstrable pathology which would predispose to recurrence, such as blebs or bullae, or after definitive surgery to prevent recurrence if CT demonstrates residual blebs. Any form of definitive surgical pleurodesis is acceptable for waiver, but thoracoscopic abrasive pleurodesis performed by a Thoracic or Cardiothoracic trained surgeon, appears to offer the best combination of efficacy and minimal morbidity. Chemical pleurodesis with talc slurry, tetracycline compounds, or other pleurodesing agents is generally not acceptable for waiver. If chemical pleurodesis has been completed prior to entry into the military service or an aviation career field, a waiver may be considered on a case-by-case basis after review by the ACS.

**Table 1: Waiver potential for Pneumothorax** 

| Flying Class | Condition  | Waiver Potential | ACS Review |
|--------------|--|------------------|------------|
| (FC)         |  | Waiver Authority |            |
| I/IA         | Primary pneumothorax   | Yes+<br>AETC     | Yes        |
|              | Multiple<br>pneumothoraces or<br>pathology noted on<br>chest CT                              | Yes*+<br>AETC    | Yes        |
| II/          | Primary pneumothorax   | Yes+<br>MAJCOM   | Yes        |
|              | Multiple<br>pneumothoraces or<br>pathology noted on<br>chest CT                              | Yes*+<br>MAJCOM  | Yes        |
| III/SWA      | Primary pneumothorax   | Yes+<br>MAJCOM   | Yes        |
|              | Multiple<br>pneumothoraces or<br>pathology noted on<br>chest CT                              | Yes*+<br>MAJCOM  | Yes        |
| GBO/ATC      | Recurrent spontaneous pneumothorax, when the underlying defect is not correctable by surgery | Yes<br>AFMRA     | No         |

<sup>\*</sup> If definitive surgery has been performed with resolution of symptoms.

AIMWTS review in Aug 2016 revealed 111 aircrew members with an aeromedical summary and the diagnosis of spontaneous pneumothorax (traumatic and iatrogenic cases were excluded). There were 29 FC I/IA cases, 40 FC II cases, and 42 FC III cases. Of the 22 disqualified (5 FC I/IA, 4 FC II, and 13 FC III), 3 were due to the aviator's voluntary decision not to pursue definitive treatment in order to become eligible for a waiver; 8 of the disqualified individuals had no other disqualifying conditions.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

<sup>+</sup> Indefinite waiver possible after ACS verification that CT imaging is without demonstrable pathology which would predispose to recurrence.

The AMS for the initial waiver for pneumothorax should include the following:

- A. A complete history of the event to include any possible predisposing factors.
- B. Documentation of all treatments given.
- C. Labs/Imaging: Reports of all imaging exams. CT chest imaging required with the actual images forwarded to the ACS for formal review.
- D. Copies of all operative reports and a statement from treating physician.
- E. Spirometry results including pre- and post-bronchodilator challenge, lung volume and DLCO studies by plethysmography.

In cases not felt to be appropriate for indefinite waiver by the ACS, the AMS for <u>waiver renewal</u> for pneumothorax should include the following:

- A. Interval history specifically noting any symptoms, changes in disease course and treatments since the last waiver submission.
- B. Current CT chest imaging with actual images forwarded to the ACS for formal review.
- C. Statement of patient condition from treating physician.
- E. Spirometry results including pre- and post-bronchodilator challenge, lung volume and DLCO studies by plethysmography.

### III. Overview.

Spontaneous pneumothorax is best defined as "air in the pleural space of non-traumatic cause." Secondary spontaneous pneumothorax is one that occurs in the presence of underlying parenchymal or airway disease, and for aviation purposes will not be considered further. Primary spontaneous pneumothorax, by default, is one that occurs in the absence of such underlying disease. However, it would be incorrect in such cases to define the lung as normal, since the vast majority prove to have visceral subpleural blebs at thoracoscopy. Most cases of primary spontaneous pneumothorax occur at rest, and it is actually unusual to see cases in the athletic realm. <sup>3, 4</sup>

Primary spontaneous pneumothorax typically peaks in the 10 to 30 year age group, affecting males about 5 to 10 times more frequently than females. The age-adjusted incidence in males and females varies widely in the clinical literature with reported rates from 7.4 per 100,000 in United States to 37 per 100,000 in United Kingdom.<sup>5</sup> It occurs primarily in tall, thin individuals and is rare in those over the age of 40. Smoking has been shown to increase the risk of primary spontaneous pneumothorax by a factor of 20 in a dose-dependent manner. More than 20,000 new cases of spontaneous pneumothorax occur each year in the United States at a cost of more than \$130 million (2006 costs).<sup>6</sup> Although the incidence in the general population is usually quoted as 9 per 100,000, the real incidence is probably higher.<sup>7</sup> In most large series, 1% to 2% are incidentally found on chest film; since small pneumothoraces resolve themselves within a few days, the odds of identifying an asymptomatic pneumothorax in this way are slim, arguing that the disease is probably more common than thought.<sup>8</sup> Fortunately, primary spontaneous pneumothorax has low mortality, with death rare in those cases occurring below age 50.<sup>9</sup>

The classic presentation in a symptomatic patient with spontaneous pneumothorax is dyspnea and pleuritic chest pain. The chest pain is almost always ipsilateral and may radiate to the shoulder, neck, and into the back. Physical exam may demonstrate tachycardia, tachypnea, hyperresonance to percussion, diminished breath sounds, and asymmetrical chest wall expansion may be present.<sup>4</sup> There are also a multitude of possible ECG changes that can be seen in the setting of a

pneumothorax. The diagnosis is best confirmed with a standard chest film. Expiratory films are no more sensitive than inspiratory films in detecting pneumothoraces and are not recommended unless there is high clinical suspicion of pneumothorax and the inspiratory film is non-diagnostic. If present on the chest film, it will demonstrate a pleural line.<sup>1</sup>

A specific subcategory that deserves mention is catamenial pneumothorax. This is a spontaneous pneumothorax occurring in a female within 48 to 72 hours of the onset of menses. Although these are often ascribed to endometriosis, pleural endometrial implants have been identified in only a third of patients. It is important to question any female with a spontaneous pneumothorax about the timing in relationship to menses, since the initial treatment of catamenial pneumothorax is hormonal. Should the patient fail a trial of contraceptive steroids, this disorder responds well to the same prophylactic surgical treatments described below.<sup>10</sup>

The major issue with spontaneous pneumothorax is recurrence. After an initial pneumothorax, the chance of recurrence in the absence of definitive treatment is 20 to 50%, a risk which probably rises after subsequent episodes. (some researchers have shown that after two pneumothoraces, the risk of a third is 62%; of those who have had three episodes, 83% will have a fourth). The clinical standard of care for a number of years has been to perform a definitive surgical procedure after the second pneumothorax, but with the availability of thoracoscopic pleurodesis, there are many who feel that surgery is indicated after the first episode, particularly in those who are at high risk because of their occupation or because of travel to remote areas.

Depending on the size of the pneumothorax, acute treatment may consist of observation, usually combined with oxygen, which hastens resolution (rate of pleural air absorption in the absence of supplemental oxygen is 1.25%/day; this is increased 3-4X in the presence of supplemental oxygen); simple aspiration of the air, which is successful about 65% of the time; or catheter or tube thoracostomy. There has been discussion for many years as to the emergency management of spontaneous pneumothorax. For many years, the gold standard was insertion of a chest tube (tube thoracostomy). Recent evidence indicates that needle aspiration is at least as safe and effective as tube thoracostomy and also carries the benefit of fewer hospital admissions and shorter length of hospital stay. Some emergency departments have begun to adopt ambulatory care treatment in small uncomplicated cases of pneumothorax. This is accomplished through the use of a one way Heimlich valve. While data for this treatment is limited, it offers the obvious advantage of eliminating an admission, and provides improved patient comfort. 14

The definitive procedure until relatively recently was chemical pleurodesis which was accomplished via the chest tube by inserting a sclerosing substance into the pleural space causing the pleura to adhere to the chest wall thereby preventing recurrences. The most common substances used were tetracycline derivatives or talc slurry. The recurrence rate with each of these was not totally acceptable and also was potentially fraught with unacceptable side effects. Problems with talc range from pain and fever to respiratory failure and ARDS. The newer and more successful interventions are surgical and include video assisted thorascopic surgery (VATS) or open thoracotomy. These procedures can lead to recurrence prevention by either mechanical abrasion pleurodesis or pleurectomy. In

# IV. Aeromedical Concerns.

The most likely symptoms are chest pain and dyspnea, either of which could be incapacitating in aircrew. There is also the concern with gas expansion at altitude in untreated pneumothorax in aviators, in accordance with Boyles Law.<sup>15</sup> The level of expansion can be calculated using Boyles equation P1V1=P2V2. For example, assuming a total lung volume of 6 L and a one sided 20% pneumothorax traveling from sea level to 8000 ft: (760 mmHg)(600 mL)=V2(567 mmHg), then V2=804 mL or approximately a 33% expansion. Given the above calculation it is possible that the gas expansion may cause significant physiological deficit.<sup>9</sup> In a review of 112 aviators with spontaneous pneumothorax, 37% admitted they could have been incapacitated had the episode occurred during flight. Overall, seventeen percent of the episodes occurred under operational conditions. Eleven percent actually occurred during flight, although it was unclear how many of these resulted in mission aborts. Of note, another 6% occurred in the altitude chamber, and all but one of those occurred after rapid decompression.<sup>3</sup>

| ICD-9 codes for Pneumothorax |  |  |  |
|------------------------------|--|--|--|
| 512                          | Pneumothorax   |  |  |
| 512.0                        | Spontaneous tension pneumothorax                                 |  |  |
| 512.1                        | Iatrogenic pneumothorax  |  |  |
| 512.8                        | Other spontaneous pneumothorax                                   |  |  |
| 860                          | Traumatic pneumothorax and hemothorax                            |  |  |
| 860.0                        | Traumatic pneumothorax without mention of open wound into thorax |  |  |

| ICD-10 codes for Pneumothorax |                                    |  |  |  |
|-------------------------------|------------------------------------|--|--|--|
| J93.11                        | Primary spontaneous pneumothorax   |  |  |  |
| J93.0                         | Spontaneous tension pneumothorax   |  |  |  |
| J95.811                       | Postprocedural pneumothorax        |  |  |  |
| J93.12                        | Secondary spontaneous pneumothorax |  |  |  |
| S27.2XXA                      | Traumatic hemopneumothorax         |  |  |  |
| S27.0XXA                      | Traumatic pneumothorax             |  |  |  |

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# WAIVER GUIDE

Updated: Feb 2017

Supersedes Waiver Guide of Feb 2014

By: Lt Col Elizabeth Casstevens (RAM 18), and Dr Dan Van Syoc

Reviewed by Lt Col Irene Folaron, AF/SG consultant for Endocrinology and Lt Col Jason

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## **CONDITION:**

Polycystic Ovary Syndrome (PCOS) (Feb 2017)

### I. Waiver Consideration.

Polycystic ovarian syndrome (PCOS) is potentially disqualifying for all classes of flying and special duty in the US Air Force. This diagnosis is not specifically mentioned in the MSD, but is covered under various other GYN topics. PCOS is disqualifying per MSD when it results in symptomatic and persistent ovarian cysts, symptomatic menstrual irregularities, or when the condition requires treatment beyond OCPs, all of which are common, and all of which are usually present when the actual diagnosis is made. The disqualification concern is similar to symptomatic and persistent ovarian cysts and abnormal uterine bleeding. If these symptoms are mild, resolved, and controlled with OCPs, they are also not disqualifying. The issues with PCOS are its association with insulin resistance, an increased risk of endometrial cancer, requirements for treatment beyond OCP, and closer follow up. Although OCPs are the most common treatment, metformin has become a standard treatment to address the insulin resistance, as well as its stronger effect on lowering serum androgen levels. Members are disqualified when the condition results in an inability to perform normal duties, results in frequent absences from duty, there is a need for use of medication requiring a waiver (such as metformin), or there is a need for ongoing specialty follow-up more than annually. PCOS can be considered for waiver if its symptoms are well controlled without medication, or with aircrew-approved medications that are well tolerated and without significant side effects.

Oral contraceptives are approved after a seven-day grounding period. The aeromedical concerns for oral contraceptives containing estrogen include risk of hypertension, increased risk of clotting in women with a history of thrombosis or concurrent tobacco use, and a contraindication in women with a history of migraine headaches with aura due to a significantly increased risk of stroke. Spironolactone is approved for use, but requires a non-high performance aircraft waiver restriction and monitoring for side effects and hypotension. Metformin is approved for use in aircrew (FC I/II/III/ATC/GBO/SWA) and also requires waiver and monitoring. Oral clomiphene citrate is also approved for aircrew use and also requires waiver and monitoring; however, it is approved specifically for infertility, not to treat PCOS. Other medications used to treat PCOS are currently not approved for use by Air Force aviators, but in some cases can be used on a case by case basis. For those medications approved for the treatment of PCOS, refer to the Aircrew and GBO Approved Medication List for the appropriate DNIF/DNIC/DNIA duration and other waiver requirements.

**Table 1: Waiver potential for PCOS** 

| Flying Class (FC) | Condition | Waiver Potential** Waiver Authority |
|-------------------|-----------|-------------------------------------|
| I/IA              | PCOS      | Yes                                 |
|                   |           | AETC                                |
| II/III            | PCOS      | Yes                                 |
| ATC/GBO/SWA       |           | MAJCOM*                             |

<sup>\*</sup>Waiver authority for initial FC II, FC III and ATC/GBO/SWA candidates is AETC.

AIMWTS search in Nov 2016 revealed a total of 88 submitted cases. There were 5 FC I/IA cases, 25 FC II cases, 1 RPA case, 39 FC III cases, 11 ATC/GBC cases, and 7 MOD cases. Of the total, 20 resulted in a disqualification disposition; 1 FC I, 3 FC II, 15 FC III cases and 1 ATC/GBC. Eight of the disqualified cases were related to the PCOS diagnosis or the medication utilized.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for PCOS should include the following:

- A. Aeromedical disposition and waiver submission should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. List and fully discuss <u>all</u> clinical diagnoses and medications requiring a waiver.
- B. A complete history to include a detailed menstrual history and an outline of the onset, duration, and stability of any symptoms of PCOS and its treatment.
- C. Exam should include assessment of blood pressure, body mass index, careful skin exam, and waist circumference. Include report of a current gynecological exam.
- D. Labs: HCG, CBC, fasting blood glucose, 2-hour (75g) glucose tolerance test, prolactin, thyroid studies, total/free testosterone, DHEAS, and any other endocrine studies used to evaluate for PCOS and its complications.
- E. Radiology: current pelvic ultrasound report and any other pertinent radiological report.
- F. Statement from treating physician summarizing treatments and intended follow-up.

The AMS for waiver renewal for PCOS should include the following:

- A. Interval history specifically noting any changes in disease course and treatments since the last waiver submission.
- B. Documentation of all exam elements.
- C. Labs: any completed since last waiver submission.
- D. Radiology: reports of pertinent exams completed since last submission.
- E. Report of current exam with statement of patient condition from treating physician.

<sup>\*\*</sup>Waiver candidates on medication must be utilizing authorized medications.

### III. Overview.

PCOS is the most common endocrine disorder in reproductive-aged women, affecting between 6.5% and 8% of all women. It is an important cause of menstrual irregularity and androgen excess in females. Its etiology is unknown and its treatment is generally empirical and symptom-based. The common manifestations include hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. It is typically characterized by irregular menses, hirsutism, acne, and obesity. Several professional groups have proposed diagnostic criteria for PCOS, using the criteria of ovulatory dysfunction, hyperandrogenism, polycystic ovaries in varying combinations with the exclusion of other disorders. The National Institutes of Health (NIH) Evidence-based Methodology Workshop Panel on PCOS suggested renaming the disorder to more adequately reflect the complex interactions between the metabolic, hypothalamic, pituitary, ovarian, and adrenal systems that characterize this syndrome and maintain the NIH and Rotterdam inclusion diagnostic criteria.<sup>4</sup> The 1990 NIH conference on PCOS developed the following minimal criteria for the diagnosis of PCOS: 1) menstrual irregularity due to oligo- or anovulation, 2) evidence of hyperandrogenism, whether clinical (hirsutism, acne, or male-pattern balding) or biochemical (high serum androgen concentrations), and 3) the exclusion of other causes of hyperandrogenism and menstrual irregularity, such as congenital adrenal hyperplasia, androgen-secreting tumors, and hyperprolactinemia. In 2003, revised criteria were developed at the American and European consensus meeting in Rotterdam. These criteria encompass a broader spectrum of phenotypes considered to represent PCOS. In the revised criteria, two out of three of the following are required to make the diagnosis: 1) oligo- and/or anovulation, 2) clinical and/or biochemical signs of hyperandrogenism, and 3) polycystic appearing ovaries on ultrasound.<sup>5, 6</sup> The Dec 2013 Endocrine Society Clinical Practice Guideline recommends using the Rotterdam criteria for diagnosing PCOS.<sup>7</sup> The evolving diagnostic criteria reflect the varying clinical findings and incomplete knowledge of the exact etiology and pathophysiology of PCOS. Many patients have evidence of abnormal luteinizing hormone (LH) secretion and a significant percentage of PCOS patients display insulin resistance. Some suggest that insulin resistance may be part of the PCOS etiology as hyperinsulinemia induces androgen secretion from the ovary and adrenal gland, and decreases sex hormone binding globulin (SHBG), which in turn increases the bioavailability of the androgens.<sup>9</sup> Although obesity is a common comorbidity and acts to amplify the effects of the disorder, it is not included in diagnostic criteria and not found in up to 20% women with PCOS.<sup>1</sup> Additionally, the prevalence of depression is up to four times higher in women with PCOS compared to women without PCOS. 10

PCOS patients experience increased ovarian androgen biosynthesis as a result of abnormalities occurring at all levels of the hypothalamic-pituitary-ovarian axis. PCOS is both a reproductive and metabolic disorder, with significant psychological manifestations as well. In the fertility arena, PCOS accounts for 70% of anovulatory infertility and probably accounts for up to 20% of infertile couples. The menstrual irregularity typically manifests at the time of menarche in PCOS women, and menarche may even be delayed. The manifestations of PCOS may be masked and its diagnosis delayed as a result of the empiric initiation of effective treatment with oral contraceptive for unexplained abnormal uterine bleeding at an early age. The chronic anovulation seen in PCOS is associated with an increased incidence of dysfunctional uterine bleeding, endometrial hyperplasia, and possibly endometrial cancer. These women also have many features of the metabolic syndrome with a strong propensity to develop type 2 diabetes mellitus (T2DM), which makes it important to diagnose and treat at an early age due to the many long-term risk factors

related to diabetes.<sup>13</sup> From the psychological standpoint, there is evidence that women with PCOS are more likely to have mood disorders to include depression and anxiety, an impaired quality of life, and higher emotional distress scores compared to women of similar BMI without PCOS.<sup>14, 15</sup> The multiple ovarian cysts, increased ovarian mass, abnormal uterine bleeding, and mood effects each or in combination may be associated with pelvic pain. Women with PCOS, also have higher rates of miscarriage.<sup>16</sup>

Patient evaluation should include a detailed menstrual history and an outline of the onset and the duration of any hyperandrogenism symptoms. The exam should include assessment of blood pressure, body mass index, and waist circumference. The skin should be examined closely for evidence of insulin resistance (which may manifest as acanthosis nigrans or skin tags) and hyperandrogenism (evidence of hirsutism, acne, and male-pattern hair loss). Lab tests are performed to confirm the diagnosis as well as to exclude other etiologies. Glucose tolerance should be assessed with a fasting blood glucose followed by a two-hour glucose tolerance test (75g), where the glucose tolerance test has a better sensitivity for glucose intolerance in PCOS. All patients should have a pregnancy test, TSH, and prolactin level to exclude other common causes of anovulation. Serum androgen testing should include total and free (bioavailable) testosterone concentrations and dehydroepiandrosterone sulfate (DHEAS) level. 75% of testosterone is from the ovary, whereas 90% of DHEAS originates from the adrenal gland. An elevated DHEAS may indicate an adrenal dysfunction such as congenital adrenal hyperplasia (CAH) or Cushing syndrome. CAH can be ruled out by measuring an AM serum 17-hydroxyprogesterone concentration. Cushing syndrome may be ruled out with a 24-hour urinary free cortisol level.

Treatment of PCOS depends on the most troubling symptoms and whether or not the patient is seeking fertility treatment. If overweight or obese, weight loss can greatly ameliorate many of the symptoms; in women with PCOS and obesity, weight loss can prompt improved ovulatory function and menstrual cycles. Regarding androgen excess, oral contraceptives are the treatment of choice for members who are not desiring pregnancy. Oral contraceptives suppress ovarian production of testosterone and, additionally, induce increased levels of SHBG, which preferentially bind androgens. Therapy typically begins with a preparation containing 30 to 35 mcg of ethinyl estradiol combined with a progestin with minimal androgenicity. Oral contraceptives can also provide endometrial protection. In addition, spironolactone can decrease hirsutism by blocking peripheral androgenic effects, although it is not FDA approved for that purpose. The insulin resistance seen in many of these patients is first addressed by lifestyle modifications such as weight loss, diet, and exercise. However, insulin-sensitizing agents, such as metformin, have been shown to improve hirsutism, obesity, and glucose intolerance.<sup>12, 17</sup> Metformin was formally approved for use in aviation in late 2010.

Metformin has been highly utilized over the past decade to treat women with PCOS. It acts indirectly and modestly to improve ovulation and to reduce long-term metabolic complications. It also acts to reduce the circulating levels of many markers of atherosclerosis and subclinical chronic inflammation. The target dose of metformin is 1500 to 2500 mg daily, and most clinical responses are not seen in doses less than 1000 mg daily. The most common side effects are gastrointestinal: diarrhea, nausea or vomiting, flatulence, indigestion, and abdominal discomfort. Lactic acidosis has been described, but is extremely uncommon in otherwise healthy subjects. Cimetidine competes for renal clearance with metformin and can cause an increase in metformin levels. Finally, 10% to 30% of patients develop vitamin B<sub>12</sub> malabsorption with decreased serum

concentrations of the vitamin. In most patients, this does not create a problem and subsequent anemia is rare.<sup>8</sup> In the aviator population, there is concern with hypoglycemia with the use of metformin. Studies of metformin in the absence of T2DM do not appear to demonstrate hypoglycemia of any level and metformin usage in such a setting should be safe in the aviation environment.<sup>19</sup>

For those women with PCOS who are seeking pregnancy, many clinicians recommend oral clomiphene citrate (Clomid®) to initiate ovulation. Clomiphene citrate blocks the hypothalamicpituitary-ovarian response to endogenous estrogens to increase the serum FSH concentration, which induces ovarian follicular development and ovulation. The primary indication for Clomid® is infertility in euthyroid women with normal serum concentrations of FSH and prolactin; this group includes women with PCOS.<sup>20</sup> Side effects are not dose-related and can occur at the minimum 50 mg dose. They include hot flashes, abdominal distention and pain, nausea and vomiting, breast discomfort, headaches, mood swings, and depression. Ovarian enlargement and multiple ovarian cyst development can occur, increasing the risk of subsequent ovarian torsion. Most important to the aviator, blurry vision, diplopia, and scotomata develop in 1 to 2 percent of women and are usually reversible. These conditions may persist, however, and necessitate termination of the treatment with this medication.<sup>21</sup> Clomiphene citrate treatment sometimes fails in obese, anovulatory women with PCOS and hyperinsulinemia. Other treatment options in these cases include weight loss, exercise, ovarian drilling, gonadotropin injections, and combination therapy.<sup>22</sup> Aeromedical concerns with the use of clomiphene citrate and gonadotropin injections is that although they are administered at specific times in the menstrual cycle, their side effects can occur throughout the entire menstrual cycle. Although tolerated by most women, these side effects can vary from month to month in an individual, and vary across individuals making a predictable assessment of tolerance difficult.

## IV. Aeromedical Concerns.

Most symptoms related to PCOS when mild or well controlled will usually not be problematic with aviation duties. However, if untreated or unrecognized, PCOS may lead to distracting gynecological problems such as abnormal bleeding or pain, as well as non-gynecological problems such as glucose intolerance, weight gain, mood disorders, and even atherosclerotic heart disease, all of which can be associated with significant aeromedical risk. The treatment of PCOS includes lifestyle changes, hormonal contraceptives, surgery, anti-estrogenic medications, and a variety of other less common treatments. The various medications have different safety profiles and must be considered individually. Not all medications used to treat PCOS are safe or approved for use by the flyer in the US Air Force.

| ICD-9 codes for PCOS |                                  |  |
|----------------------|----------------------------------|--|
| 256.4                | Polycystic ovaries               |  |
| 620.2                | Other & unspecified ovarian cyst |  |

| ICD-10 codes for PCOS |                             |  |
|-----------------------|-----------------------------|--|
| E28.2                 | Polycystic ovarian syndrome |  |
| N83.20                | Unspecified ovarian cyst    |  |
| N83.29                | Other ovarian cysts         |  |

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## Posttraumatic Stress Disorder (PTSD) (Jan 2020)

Reviewed: Lt Col Kevin F. Heacock (ACS Neuropsychiatry Branch Chief), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

Restructuring of Waiver Guide, Anti-depressant management, AIMWTS review

#### I. Waiver Consideration

A diagnosis of Posttraumatic Stress Disorder (PTSD) does NOT require a waiver if the member is able to return to full duty within 60 days of symptom onset (minor residual symptoms are acceptable). However, the condition is disqualifying and a waiver will be required before consideration of return to flight status if any of the following conditions are met: (a) DNIF lasts greater than 60 days; (b) member experiences a recurrence of debilitating symptoms upon return to the operational environment; or (c) original symptom severity was such that in the opinion of the flight surgeon, return to the operational environment would entail high risk to the member, the mission or flight safety should the symptoms recur. Flight surgeons caring for distressed aviators, especially in times of combat, need to be particularly sensitive to these issues and work closely with a psychiatrist or psychologist early in the evaluation, treatment and aeromedical disposition of these aviators whether or not their symptoms are caused by combat/operational stress or other traumatic incidents.

To be considered for waiver, a mental health evaluation, with accurate diagnosis per the DSM-5, is the vital first step. USAF psychologists/psychiatrists familiar with aeromedical standards are the preferred choice for evaluation and potential development of the treatment plan. Most waivers granted to date have been limited to those with six months of sustained remission. Mild, residual symptoms, not thought to be duty impacting, are relatively common and acceptable.

In 2013, the USAF began allowing select FC II/III personnel to be considered for waivers on antidepressants. After 5 years of observation, in 2018 the USAF allowed all aviators, including single seat and B-2 pilots, to be considered for waivers on the following monotherapies:

- 1. Sertraline (Zoloft®) up to 200 mg/day
- 2. Citalopram (Celexa®) up to 40 mg/day
- 3. Escitalopram (Lexapro®) up to 20 mg/day
- 4. Bupropion (Wellbutrin®) SR or XL up to 400 mg/day or 450 mg/day, respectively

Of these approved medications, Wellbutrin is known to be less effective in treating PTSD. Also, the dosage of the antidepressant tends to require "higher than usual" amounts when treating PTSD as compared to treatment for depression. This often makes Zoloft an attractive choice in treating PTSD among these approved antidepressants.

The aviator on a maintenance antidepressant (only one aeromedically approved medication allowed) needs to be on the medication and remain clinically asymptomatic for at least 6 months before

waiver consideration. The dose of the medication can be adjusted to maximize treatment and/or limit side effects without restarting this 6-month period as long as the aviator's symptoms remain stable. If a psychotropic medication is ever adjusted in dose or discontinued in an aviator, two weeks of observation should occur before considering resuming full flight duties to assure no adverse/unexpected side effects or return of symptoms occur. If symptoms return after discontinuing treatment, a return to, or enhancement of, psychotherapy, healthy lifestyle interventions, and/or antidepressant medication for maintenance treatment should be considered.

**Table 1: Waiver potential for PTSD** 

| Flying Class (FC) | Waiver Potential   | ACS Evaluation or |
|-------------------|--------------------|-------------------|
|                   | Waiver Authority   | Review            |
| I/IA              | Maybe <sup>1</sup> | Yes <sup>2</sup>  |
|                   | AETC               |                   |
| II/III and        | Yes                | Yes <sup>2</sup>  |
| ATC/GBO/SWA       | MAJCOM             |                   |

<sup>1.</sup> Must clearly demonstrate complete resolution of all PTSD symptoms before acceptance into initial flying training and have complete documentation from mental health providers.

## **II. Information Required for Waiver Submission**

# A. Initial Waiver Request:

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder.
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

### B. Renewal Waiver Request:

- 1. See Mental Health Waiver Guide Checklist in Psychiatry Waiver Guide Folder.
- 2. If the local base is unable to provide all required items, they should explain why to the waiver authority.

## Please feel free to contact the ACS Neuropsychiatry Branch with questions:

ACS Aerospace Medicine Branch, USAFSAM/FECA

c/o Neuropsychiatry Branch <u>USAFSAM.FE.PsychiatryMailbox@us.af.mil</u>

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## **III. Aeromedical Concerns**

The diagnosis of PTSD, especially in the combat environment, is fraught with difficulty. Normal reactions to combat, operational stress, and emotional/stressful events can all be confused with and labeled as PTSD, especially when the member is routinely exposed to the stressful environment. While symptoms are similar, the course of treatment and aeromedical dispositions of the reactions are extremely different. Flight surgeons and mental health providers need to consider the length, severity, and functional impact of PTSD symptoms along with the situationally induced nature and accompanying stressors that triggered the condition.

<sup>2.</sup> Must be reviewed by the ACS prior to consideration for a waiver.

There is a high prevalence of other psychiatric disorders in individuals diagnosed with PTSD, with both men and women reporting other comorbid psychiatric conditions. Major Depressive Disorder is among the most common comorbid conditions for both men and women, affecting nearly 50%. Alcohol Use Disorder is also highly comorbid in men (seen in over half of all cases). Additionally, there is a threefold to sevenfold increased risk for both men and women with PTSD for diagnosis of Anxiety Disorders, including Generalized Anxiety Disorder, Panic Disorder, and Specific Phobias. These diagnoses should be screened for to consider flying status, treatment, and waiver potential for them as well.

Early intervention and treatment may prevent chronic disease. Long-term multifaceted treatment has shown the greatest benefit to those afflicted, given the complex nature of PTSD. Various psychotherapeutic modalities have been shown to be effective in PTSD. Prolonged Exposure, Cognitive Processing Therapy (CPT), and Eye Movement Desensitization and Reprocessing (EMDR) therapy have been found effective in randomized trials. Psychotherapy, along with healthy lifestyle modifications, are the treatment of choice for PTSD. It is advisable for primary care providers and flight surgeons to refer these patients to a therapist or treatment team with experience in such therapies.

The therapeutic goals of psychopharmacologic therapy are to decrease intrusive thoughts and images, phobic avoidance, pathological hyperarousal, hypervigilance, impulsivity, and depression. Selective Serotonin Reuptake Inhibitors (SSRIs) were found to be effective as first-line drug therapy in a systematic review of 35 randomized trials and are recommended in treatment guidelines for PTSD from the American Psychiatric Association. SSRIs have been found to reduce flashbacks, arousal, and avoidance in patients with PTSD.

Prolonged severe operational stress can cause symptoms of PTSD. For operational stress reactions, the individual's symptoms typically clear shortly after removal/restriction from duty. Specific situational anxiety reactions that develop after traumatic incidents (e.g. claustrophobia, flying phobia), when symptoms do not interfere with duty, are best treated with occupational exposure with or without short term DNIF. In situations in which exposure-based therapies would facilitate resolution of symptoms, prolonged restriction from duty may actually delay recovery.

In some instances, a member's symptoms are more generalized, accompanied by a change in social or occupational functioning, and do not clear with time off, adequate sleep and initial treatment attempts. In these cases, consider the diagnosis of PTSD, other associated conditions, and the member's motivation. Many of the symptoms of PTSD can interfere with flying safety and mission completion. Severe anxiety symptoms markedly impair the ability to focus and concentrate on the task at hand. Some of the more severe symptoms, such as flashbacks, may be acutely incapacitating. Associated mental health conditions can also negatively affect the ability of the aviator to successfully complete the mission. DNIF and treat whenever symptoms interfere with safety of flight, the mission, or the member's safety, regardless of diagnosis.

Remotely Piloted Aircraft (RPA) operators and others involved in remote warfare have the potential to develop PTSD through their viewing of work-related video and other electronic media. Recent efforts to investigate the prevalence of PTSD in the remote warfare community suggest rates of

PTSD are similar to other USAF pilots and lower than the general population. To this point, few cases of PTSD as a direct result of RPA operations have been reported.

AIMWTS review in Jan 2020 for the previous five years revealed 246 airmen with a diagnosis of PTSD, with 158 of the cases resulting in a disqualified disposition. Breakdown of the cases revealed: 9 FC I/IA cases (4 disqualified), 40 FC II cases (24 disqualified), 11 RPA cases (8 disqualified), 123 FC III cases (77 disqualified), 31 ATC/GBC cases (25 disqualified), 29 Special Warfare airmen (18 disqualified), and 3 MOD cases (2 disqualified). The major factors resulting in a disqualification were persistent symptoms, chronic disease, other mental health diagnoses, and the need to treat with medications not approved for use in USAF aircrew.

| ICD-9 code for PTSD |                                |
|---------------------|--------------------------------|
| 309.81              | Post-traumatic stress disorder |

| ICD-10 codes for PTSD |   |  |  |
|-----------------------|---|--|--|
| F43.10                | Post-traumatic stress disorder, unspecified |  |  |
| F43.12                | Post-traumatic stress disorder, chronic     |  |  |

## IV. Suggested Readings

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## Pregnancy (Sep 2019)

Reviewed: Mike Acromite (OB/GYN & former ACS staff physician), Col Justin Nast (OB/GYN, Flight Surgeon), Lt Col Jason Massengill (AF/SG OB/GYN consultant), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

## **Significant Changes:**

Updated criteria for clearance approval, base SGP can approve clearance for uncomplicated pregnancies, expanded timeframe for flying allowed, RPA Pilots/SO no longer need DNIF if uncomplicated, new format

## I. Clearance to Fly/Operate Consideration

Pregnancy is a temporary grounding condition for FC I, IA, II, III, OSF and SWA duties. Uncomplicated pregnancies do not require a waiver for continued duties for GBO and ATC throughout the duration of pregnancy. (Complicated pregnancies require grounding and may potentially be waived.) Pregnancy is associated with typical physiological changes and pregnancy-specific conditions that can adversely affect the female pilot's flying performance, safety, and her pregnancy (see Aeromedical Concerns, Section III). Most females and their pregnancies however, can tolerate flying conditions with appropriate mission and safety considerations. For all flying classes, duty modification should be considered in cases where the time to urgent obstetrical care is greater than 2 hours, or a shorter time appropriate for the condition of the pregnancy. (Aerospace Physiology training is prohibited during pregnancy, but extensions to the training may granted during pregnancy, per AFI 11-403, *Aerospace Physiological Training Program*. See section E).

Table 1: Flying/Operational Clearance Potential<sup>4</sup>

| Flying Class | Condition   | Clearance Allowed<br>Waiver Authority |
|--------------|---|---------------------------------------|
| I/IA         | Pregnancy   | No                                    |
|              |   | AETC                                  |
| II/III       | Pregnancy - 12 <sup>th</sup> through 28 <sup>th</sup> | $Yes^1$                               |
|              | gestational weeks <sup>2</sup>                        | Base - uncomplicated                  |
|              |   | MAJCOM -                              |
|              |   | complicated                           |
| GBO          | Pregnancy through delivery <sup>3</sup>               | No DNIF/DNIA –                        |
|              |   | uncomplicated                         |
|              |   | MAJCOM -                              |
|              |   | complicated                           |
| ATC          | Pregnancy through delivery <sup>3</sup>               | No DNIC -                             |
|              |   | uncomplicated                         |
|              |   | MAJCOM -                              |
|              |   | complicated                           |
| SWA          | Pregnancy at any time                                 | No                                    |
|              |   | N/A                                   |

<sup>1.</sup> FC II/III aircrew are allowed to fly in non-ejection seat aircraft, pressurized to at least or which naturally do not fly higher than 10,000 MSL, with another qualified pilot. For aircraft and pregnancies that do not meet all of the above guidelines, waiver will not be considered.

- 2. Other than designated gestational period, flying not allowed.
- 3. Duty limiting profiles must be considered for physical limitations and geographic considerations as appropriate throughout the pregnancy
- 4. ACS review is not required for pregnancy cases. However, MAJCOM SGPs may request OB consultant and/or ACS help in adjudicating complicated cases.

**FC II, FC III**: Trained aircrew will be DNIF automatically upon learning of pregnancy. Specified aircrew (FC II/III – no flying clearance potential for aircrew in training status) can be returned to flight duties without a waiver if the following conditions are met:

- 1. The request to fly is voluntary and must be initiated by the crewmember.
- 2. The pregnancy must be uncomplicated/low risk, with validation from appropriate level obstetrical provider and the flight surgeon.
- 3. Flying is restricted to non-ejection seat aircraft in which cabin altitude remains at or below 10,000 feet MSL (pressurized or naturally). Pilots require another qualified pilot (except RPA).
- 4. The flying period is valid from the 12<sup>th</sup> through 28<sup>th</sup> week of gestation.
- 5. Crewmembers are released from mobility commitments.

**GBO, ATC**: Although uncomplicated pregnancy is not disqualifying for GBO and ATC duties, it may be appropriate to remove an individual from her duties if she is experiencing pregnancy-related side effects that affect the safe performance of her duties. Official duties activities may require females to travel for several hours to locations very remote from urgent obstetrical care. Duty modification should be considered in cases where the time to urgent obstetrical care is greater than 2 hours, or a shorter time appropriate for the condition of the pregnancy. Complicated pregnancies in GBO and ATC personnel should be treated as disqualifying. Waivers to continue duties can be considered at the MAJCOM level, with consultation with the ACS and/or OB consultant as needed.

**SWA**: Pregnancy is disqualifying for Special Warfare duties at any time in the pregnancy and they will remain off status through 6 months post-partum.

Uncomplicated Pregnancy: The pregnancy must be a singleton and considered uncomplicated. An uncomplicated pregnancy is one without significant abnormal physiological changes or significant pregnancy-specific conditions. Prenatal labs and vital signs must be normal, and an obstetrician must verify the uncomplicated pregnancy. Aviator age at time of delivery must be less than 35 years old. (Women who are considered "Advanced Maternal Age," above age 35 at time of delivery, are higher risk for complications, including miscarriage, stillbirth, and genetic anomalies.) Preexisting medical conditions, medications, and waivers must be reconsidered in the context of the pregnancy. Previously scarred uterus (cesarean delivery or other uterine surgery) may affect the risk to the pregnancy and aviation environment and should be addressed by the Obstetrician. Note: multi-gestation pregnancies have higher risks for more dynamic physiological changes, preterm labor, preeclampsia, gestational diabetes, pain, hyperemesis, and more significant ergonomic factors.

**Postpartum**. After delivery, returning an aviator to flying status is considered following a minimum of six weeks post-partum, and then as soon as practical. It may be longer depending on mode of delivery and any complications. Consider the potential risks in the post-partum period including post-partum depression, bleeding, surgical complications, blood pressure, infection, and glucose intolerance, as well as the persistence of the thrombophilic state for up to six weeks after delivery.

## II. Information Required for Flying/Operational Clearance or Waiver Process

Evaluation for potential clearance for flying/operational duties while pregnant should initially start with the "Pregnancy in Aviators/Operators Flowchart." The flight surgeon must ensure that the aviator is voluntarily requesting to continue flying (by using the "Aviator's Request to Fly While Pregnant" document). Aviators must bring the "OB Pregnancy Verification" form to their OB at their initial visit to confirm the pregnancy is low risk/uncomplicated. These documents, attached at the end of this waiver guide chapter, will aid in assuring the flyer and medical providers understand the factors and their risks that must be considered. If the reviewing flight surgeon and obstetrician deem the pregnancy to be low risk, the aircraft is appropriate, and the aviator documents her desire to fly after reviewing the risks, the above listed three documents will be brought to the base SGP for review and approval. The member can be returned to fly between 12 through 28 weeks. The documents will be scanned and placed in the electronic medical record repository (HAIMS). While pregnancy is not strictly disqualifying for GBO and ATC, the flight surgeon should also take into account pregnancy related conditions and individual risk factors when managing duty restrictions. Pregnancies with medical co-morbidities are not considered low risk and therefore require a waiver for the aviator. Waivers require MAJCOM level approval. If an aviator has a flying waiver for another condition in an otherwise normal pregnancy, this needs to be taken into account by the base SGP when evaluating if clearance is appropriate at base level, or if a MAJCOM level review is needed.

Follow up. While pregnant and flying, the aviator will return to the Flight and Operational Medical Clinic every four weeks (ideally timed right after each OB visit) for an evaluation, including, at a minimum:

-Continued desire to fly.

- -Visual acuity check\* (vision correctable to 20/20).
- -Vital sign evaluation.
- -No development of any condition impairing wear of safety equipment or in-flight safety or emergency egress.
- \* Required for FCII/III and ATC, but not for GBO.
- -At any time during the pregnancy, if a complication or situation arises making the pregnancy high risk, and <u>after each OB clinic visit</u>, the aviator/operator must present to and notify her Flight Surgeon of status for determination if continued flight/operator status is appropriate.

For any pregnancies that are not deemed to be low risk, and a waiver is requested, an aeromedical summary (AMS) will be submitted to the MAJCOM for review in the usual fashion. For pregnancies that are low risk, but the aviator already has a waiver for an unrelated condition, the SGP can determine if the waiver needs to be approved at the MAJCOM level. The AMS should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations. It is important to take into consideration that aviators requesting to fly while pregnant have a short window of eligibility (in the 2<sup>nd</sup> trimester). Therefore, every effort should be made to have the AMS assembled and submitted to the MAJCOM for review as quickly as possible.

# The AMS must include the following:

- 1. Flying class (or special duty), aircraft, location, (note: necessary level of obstetrical care availability). Expiration date of Aerospace Physiology training qualifications.
- 2. Date of pregnancy confirmation, estimated current gestational age, and estimated date of delivery, verification of normal singleton intrauterine pregnancy.
- 3. Date of start of 12<sup>th</sup> week of gestation (start of waiver eligible period) and date of end of 28<sup>th</sup> week of gestation (end of waiver eligible period).
- 4. Current status of pregnancy: any significant symptoms, or significant conditions.
- 5. Past obstetrical history (pregnancies (dates), delivery type, complications, etc.) and past gynecological history (ectopic pregnancy, miscarriages, fibroids, dysplasia, etc.).
- 6. Past medical and surgical histories.
- 7. Aeromedical history to include preexisting condition (and current status), medication, including changes due to pregnancy, and any other existing waivers.
- 8. Physical: documentation from the obstetrical provider, including: blood pressure, visual acuity (reassess every 4 weeks, or sooner for flyer symptoms), pelvic findings (absence of cervical changes or bleeding), and ultrasound findings.
- 9. Labs: CBC, urinalysis and urine culture, and any other standard initial pregnancy labs.
- 10. Statement that the obstetrical provider has documented an uncomplicated pregnancy in the context of aeromedical concerns and agrees with the request for waiver to continue flying during pregnancy. ("OB pregnancy verification.")
- 11. Statement that the waiver request was voluntarily initiated by the aviator, that she understands the potential risks of flying duties while pregnant, and that any changes in her status require follow-up with flight medicine prior to resuming flight duties. ("Request to fly while pregnant.")
- 12. Statement that her flight surgeon agrees with request for waiver to continue flying during pregnancy.

- 13. Statement regarding automatic disqualification from and prohibition of Aerospace Physiology training until pregnancy is completed and member returned to flight status.
- 14. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Pregnancy is associated with typical physiological changes, pregnancy-specific diseases, effects on preexisting medical conditions, and effects on medications, all of which individually and in combination may be aeromedically significant. The physiological changes vary within and across pregnancies. These novel physiological states can be quite different from the female flyer's baseline physiological state experienced during initial flight training and during typical nonpregnancy flying experiences. As such, these often unperceived changes have the potential to result in unexpected, subtle, or profound physical responses to create aeromedical risks. Pregnancy related changes may cause aeromedically significant changes to the state of preexisting diseases, or its treatment, requiring reassessment. Pregnancy-specific diseases and conditions arising at various points in the pregnancy create their own aeromedical risks and conditions that are often incompatible with flying. Additionally, the physical changes of pregnancy can create occupational limitations for the flyer. Finally, the flying environment may create environmental exposure risks to the fetus. Therefore, prior to returning to the flight environment, it is essential that flyers and their medical care team are aware of these circumstances, the potential effect on flying performance and safety. It is essential to establish awareness, an accurate assessment, and appropriate monitoring methods to mitigate these risks.

There is evidence that pregnant active-duty women in general, represent a high-risk group. The scarce evidence in pregnancy for the adverse effects of aviation-related occupational exposures such as noise, vibration, jet fuel exposure, exposure to fumes, shift work, long hours, heavy lifting, hypoxia, G-force, and altitude exposure, is related to the paucity of human studies in the flying environment, especially in military flying. Despite this, the risks are real and must be individually assessed, addressed and monitored to assure a risk-appropriate flying disposition.

Pregnancy is a grounding condition for all flying classes (except ATC and GBO), with flying status possible in certain conditions, outlined in Section I. Once the pregnancy is confirmed, accurate dating must be established as early in the pregnancy as possible. The pregnancy must then be assessed by the obstetrical care provider to confirm an intrauterine location to avoid the risk of ectopic pregnancy. This is followed by a determination whether the pregnancy is considered "normal" or "high-risk" based on the pregnancy state, previous medical history, and associated conditions. A pregnancy determined to be "high-risk" initially or at any time in the pregnancy is not considered for initial or continuation of a waiver.

The decision to fly while pregnant remains a personal one for most women. In order for the flyer to continue flying duties while pregnant, the flyer, her flight surgeon, obstetrical care provider, and commander must continually collaborate to determine her specific flight risk. The flyer must personally request to continue flying after considering the condition of her pregnancy and its associated risks. The areas of concern for aeromedically risk areas are included below.

# A. Physiological Changes of Pregnancy:

**Vision**: Corneal thickening due to edema can occur as early as 10 weeks gestation, and can persist for several weeks postpartum. This change is variable, and can affect visual acuity differently throughout the pregnancy. The visual acuity should be checked every two weeks to assure vision standards appropriate for their duty are met. In addition, an immediate assessment should be performed for any visual complaint. The use of contact lenses in pregnancy is discouraged.

Hypercoagulability: Pregnancy is a hypercoagulable state with a risk of venous thrombosis or thromboembolism increased at least five-fold over the non-pregnant state. Venous thromboembolism is the leading cause of maternal deaths in developed countries. This is related to increases in fibrinogen, von Willebrand Factor, clotting factors (V, VIII, and X), and changes in plasminogen activating inhibitors 1 and 2. In addition, venous stasis is more likely due to decreased systemic vascular tone and compression of the pelvic veins by the enlarging uterus. Periods of inactivity or remaining in a cramped cockpit during flying duties can also contribute to venous stasis and the risk of thrombosis. Underlying hypercoagulable states, such as Factor V Leiden, are associated with 20-25% of venous thromboembolism in pregnancy and as such, can add substantially to the venous thrombosis risk. Screening for thrombophilia is not recommended routinely in pregnancy, but can be considered based on clinical or family history.

Hemodynamic: Blood volume increases during pregnancy to accommodate the pregnancy requirements and benefit placental perfusion. Plasma volume increases by 40%, and red cell mass increases 20-30% over the non-pregnant state. A relative anemia is common in pregnancy due to the increased ratio of plasma volume to red cell mass and resulting hemodillution. Iron deficiency anemia is also common in pregnancy due to the substantial increase in iron requirement for the growing fetus. The obstetrical care provider may tolerate lower hemoglobin and hematocrit levels considered "normal" for pregnancy, but these levels may not be adequate for a pregnant aviator. In addition, the intravascular blood volume can decline during pregnancy due to decreased venous tone and extravascular fluid shifts as edema. Changes in maternal pH from respiratory changes cause a right shift in oxygen dissociation of hemoglobin to facilitate oxygenating the fetus. These volume, hemoglobin, and anemia-related circumstances can affect a flyer's G-tolerance, vision, endurance, fatigue, and tolerance for hypoxia. Monitoring of the hemoglobin and hematocrit is common in routine prenatal care, but requires additional monitoring for symptoms if flying is considered. The standard replacement of iron and folate in prenatal vitamins is generally adequate, but additional supplementation is often required.

Cardiovascular: The base-line heart rate gradually increases throughout a normal pregnancy. There is a 10-fold increase in uterine blood flow resulting in a shift from 2% of total cardiac output pre-pregnancy to over 17% at term. The growing uterus exerts pressure on the pelvic veins and vena cava that can reduce venous return and preload to the heart. Maternal posture can decrease cardiac output by 25-30%, and 8% of women experience supine hypotension with possible syncope. The vascular tone and its pressor-responsiveness to systemic requirements are suppressed in the normal pregnancy due to increased systemic progesterone, changes in prostaglandins, low resistance within the placenta, and other factors. Vascular collagen changes increase vascular compliance as early as 5 weeks of pregnancy. The vascular pressor response is decreased from renin-angiotensin refractoriness. During a normal pregnancy, the average blood pressure begins to decrease by 7 weeks of gestation, reaching a nadir by 24 to 32 weeks, gradually increasing in the third trimester,

and returning to pre-pregnancy levels following delivery. These changes can have significant or subtle effects on the pregnant flyer's cardiac performance, and in turn, can affect G-tolerance, vision, endurance, fatigue, and hypoxia tolerance.

**Pulmonary**: Pulmonary changes can be significant in the aviation environment. There is an increase in maternal oxygen consumption with a 40% increase in tidal volume and a stable baseline respiratory rate. This results in a hyperventilation, hypocapnia, and pH changes. The lung volume is decreased from physiological changes and uterine encroachment. These changes result in 20% decreases in each of the expiratory reserve volume, residual volume, and functional residual capacity, and can result in early decompensation in the face of infection, or other pulmonary disease. In the flight environment, these can affect hypoxia tolerance, especially in a situation of rapid decompression.

Renal: In pregnancy, renal blood flow increases by 50%, renal plasma flow increases by 60-80%, and glomerular filtration rate increases by 50%. The increased renal function and uterine compression of the bladder result in more urine production during a normal pregnancy. This results in more frequent urination, a higher risk of dehydration, and increased potential for kidney stones. The dry flight environment can further induce dehydration. These factors can have significant or subtle effects on the flyer's G-tolerance, vision, endurance, fatigue, or hypoxia tolerance. Elevated systemic progesterone decreases the peristalsis of the ureters to increase the risk of kidney stones, ureteral reflux, and ascending urinary tract infections. As such, urinary tract infections must be treated with more vigilance in pregnancy due to the greater risk of pyelonephritis, and its higher risk of complications.

Gastrointestinal: During normal pregnancies, high circulating levels of progesterone, a smooth muscle relaxant, causes hypoactivity of the gastrointestinal tract, a decrease transit time, relaxation of the lower esophageal sphincter, and increased vomiting. Pregnancy-associated vomiting occurs most commonly during the first trimester, but can occur throughout the pregnancy. The vomiting may become frequent enough to require anti-emetic medications. In the rare cases of hyperemesis gravidarum, the episodes become frequent and severe that parenteral fluid/nutrition is required in addition to anti-emetic medications. Although severe cases of nausea and vomiting are less common, any nausea, vomiting, and retching, can result in significant aeromedical distractions and additional dehydration.

**Endocrinology**: Pregnancy is a diabetagenic state associated with hyperinsulinemia and insulin resistance. For the mother, this can result in relative hyperglycemia or frank (gestational) diabetes. In cases of gestational diabetes, control can be achieved with diet and the use of oral hypoglycemic medication, although sometimes insulin is required. Maternal screening for diabetes generally occurs at 26-28 weeks of gestation, but may be performed earlier for risk factors or clinical findings.

**Immune System**: A normal pregnancy has changes that can suppress the immune system. This change allows the maternal system to tolerate the antigenic difference of the fetus. As a consequence, a pregnant female can be more susceptible to general infections, and infections can be more severe. More aggressive treatments may be required. Live virus vaccinations are not recommended in pregnancy, but other routine non-live vaccines are acceptable and recommended

according to the American College of Obstetricians and Gynecologists and Centers for Disease Control and Prevention (CDC).

Ergonomic Considerations: As the uterus grows during pregnancy, it emerges from the pelvis after 12 weeks and begins to increase abdominal circumference thereafter. Breast tissue enlarges in response to human chorionic somatomammotropin. Size and weight distribution changes can result in requirements for changes within the flight environment or equipment. Localized or generalized edema can occur in normal pregnancies and may increase the circumference of the lower extremities, the upper extremities, and occasionally other areas of the body. Esophageal reflux is also more common during pregnancy, particularly when recumbent. These changes may affect the fit and safety of life support equipment in the aircraft and must be considered initially and throughout the pregnancy.

**Sleep**: Sleep disturbances during pregnancy are common and can contribute to excess fatigue in the aviator. These disturbances tend to increase as the pregnancy progresses resulting in additional aeromedical significance.

Distraction/ loss of mental alertness from morning sickness, sleep disturbance, contractions, lower abdominal discomfort, increased urinary frequency and gastro esophageal reflux: Alone or in combination, these conditions might lead to distraction and a loss of situational awareness. For this reason, aviators who have been medically cleared to fly should feel comfortable and empowered to self ground. This is one important reason for frequent follow up with the flight surgeon and every effort should be made by the flight surgeon and the command to cultivate an environment that would facilitate this process.

#### **B.** Environmental Effects on the Mother and Fetus:

Heat exposure: The fetus generates additional heat. The mother is expected to gain 25-35 pounds during the pregnancy. The flight environment and safety equipment may further increase heat exposure to the flyer. The combination of increasing body mass index, the flight environment, and fetal heat generation can result in maternal heat intolerance and adverse effects to the fetus. Elevated core body temperature has been shown to double the risk of neural tube defects in the fetus. Animal studies suggest elevated ambient temperatures are associated with an increase in risk of preterm labor and growth restriction. These should be addressed when considering continuation of flight duties in these environmental conditions.

**Sound and Vibration Exposure**: Sound and vibration exposure during the second trimester has been associated with hearing changes identified in the newborn. The hearing organs are developed around 20 weeks gestation and may be susceptible to vibration and noise damage. Significant noise and vibration exposures have been associated with fetal growth restriction and preterm labor, possibly related to increased maternal catecholamines. The maternal abdomen, organs, placenta, and uterus have been shown to provide a modest noise attenuation in animal models. Noise frequencies less than 250 Hz are attenuated less. Limited evidence suggests exposures greater than 115 dBC 8-hour time weighted average (TWA), or 155 dBC pulse, may be associate with fetal hearing effects after 20 weeks gestation. A specific dose effect however, has not been fully elucidated, but reasonable reductions in frequency and duration of exposure can be considered when appropriate.

**Radiation Exposure**: Radiation exposure is a potential risk factor for the fetus. It is most vulnerable during organogenesis in the first trimester. Evidence suggests that no adverse fetal effects have been seen with radiation exposures of less than 50 mSv. The average exposure during a 10-hour flight is 0.05 mSv. Population based studies of pregnant commercial airline workers and the associated radiation exposure are reassuring - showing no adverse fetal outcomes, but are not necessarily applicable to military aviation.

**Altitude Exposure**: A 2014 study suggests that an increase in maternal altitude exposure may be associated with a reduction in birth weight, which increases with increasing altitude exposure. Maternal altitude restrictions are included for flight duty waiver consideration.

- C. Pregnancy-Specific Medical Conditions: Pregnancy-specific conditions can induce a "highrisk" pregnancy that is incompatible with flight duties. It is essential for the obstetrical care provider to perform a complete initial assessment, as well as subsequent assessments to identify these conditions. Prompt notification of the flyer, and her flight surgeon is necessary to identify those conditions incompatible with flying duties. Examples of pregnancy-specific "high-risk" conditions include, but are not limited to: ectopic pregnancy, spontaneous miscarriage, molar pregnancy, incompetent cervix, vaginal bleeding, advanced maternal age (>35 years old) preterm labor, spontaneous rupture of membranes, preeclampsia, hyperemesis gravidarum, gestational diabetes, struma ovarii, uterine anomaly, and fetal conditions such as multiple gestation, birth defects, growth restriction, oligohydramnios, chorioamnionitis, or others. These conditions can be associated with sudden and unexpected symptomatology, including but not limited to pain, bleeding, severe headaches, or even seizure. These can cause life-threatening conditions to the flyer, and significant adverse risk to the pregnancy and fetus. In addition, they can result in subtle or profound distraction or frank incapacitation within the flight environment. Therefore, it is of utmost importance to confirm that a pregnancy is intrauterine, normal, and remains normal throughout any period of continued flight duty.
- **D.** Preexisting Medical Conditions or Medication Use Affected by Pregnancy. There are a variety of medical conditions where the disease, the treatment, or both are affected by pregnancy. Such conditions include chronic hypertension, impaired glucose tolerance, diabetes, thyroid disease, inherited thrombophilias, migraines with aura, or history of thromboembolic disease. In many cases, a chronic medication or its dose must be changed. Therefore, when a pregnant flyer has a preexisting medical condition and/or stable use of a medication previously waived, these must be re-considered prior to returning to flying duties.
- **E. Training Qualifications**. Pregnancy is disqualifying for initial flight training and waivers are not considered. Waivers are only considered for trained aircrew. Pregnancy is considered disqualifying for physiological training, hyperbaric duty, or operational flying support. Aerospace Physiology training is prohibited during pregnancy. Waivers or deferrals are not recommended for these training requirements. However, per AFI 11-403, *Aerospace Physiological Training Program*, extensions to physiology training currency can be granted for the duration of the pregnancy. Pregnancy is disqualifying for hypobaric/hyperbaric duty as an inside observer.

| ICD-9 C | Code for Pregnancy            |
|---------|-------------------------------|
| V22     | Normal Intrauterine Pregnancy |

| ICD-10 | Code for Pregnancy |
|--------|--------------------|
| Z33    | Pregnant state     |

## IV. Suggested Readings

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# **USAF Aviator/Operator Pregnancy Flowchart**

| Name:   |  |  |  | Ag   | e:   | _ Wei  | ight:   |  |  |           |
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# Request to Fly While Pregnant

Pregnancy is a normal female condition resulting in various important physiologic changes. Many of the normal physiologic changes of pregnancy create potential risks in the US Air Force aviation environment. The overall impact of these changes is unpredictable and varies between different patients and pregnancies. In addition to the risks from a normal pregnancy, there are certain specific pregnancy related disorders that can cause sudden incapacitation or life-threatening emergencies. Furthermore, pregnancy can exacerbate other chronic medical problems. These issues present unique risks to the aviator who continues to fly during pregnancy. This document is meant to educate aviators on these risks, so she can have as much information as possible when deciding to fly while pregnant. It is not a legal consent form.

Aviators with complicated pregnancies, or certain pre-existing medical conditions (other medical waivers), should not fly while pregnant. Aviators should not fly during high risk times in the pregnancy, such as the first and third trimester. Solo flights, flights in ejection seat aircraft, and flights with risk for hypoxia or excessive G-force exposures are not allowed during pregnancy. To be considered uncomplicated/low risk, aviator age at time of delivery must be less than 35 years old, in accordance with current American College of Obstetricians and Gynecologists guidelines. (Women who are considered "Advanced Maternal Age," above age 35 at time of delivery, are higher risk for complications, including miscarriage, stillbirth, and genetic anomalies.)

The decision to fly while pregnant remains a personal one for most women. In order to continue flying duties, the aviator, her flight surgeon, obstetrical care provider, and commander must continually and coherently collaborate to determine her specific flight risk. The flyer must personally request to continue flying after considering the condition of her pregnancy and its associated risks. Some of the common physiologic changes in pregnancy and potential hazards are described below.

### **Physiological Changes of Pregnancy:**

Vision: Thickening of the front surface of the eye due to swelling can occur as early as 10 weeks into pregnancy, and can persist for several weeks after delivery. This change is variable, and can affect vision differently throughout the pregnancy. The visual acuity should be checked every two weeks to assure vision standards appropriate for flying duties are met. Additionally, vision should be checked by the Flight Surgeon office for any visual complaint. The use of contact lenses in pregnancy is discouraged.

Hypercoagulability: Pregnancy is a state where there is an increased risk developing blood clots, at least five-fold over the non-pregnant state. Blood clots that develop in the veins and move to the lungs is the leading cause of maternal deaths in developed countries. This is related to increases in various clotting factors. In addition, pooling of the blood is more likely due to decreased tone in the blood vessels and compression of the pelvic veins by the enlarging uterus. Periods of inactivity or remaining in a cramped cockpit during flying duties can also contribute to this pooling and the risk of blood clots. Underlying states of increased blood clots are associated with 20-25% of blood clots in veins in pregnancy and as such, can add substantially to the clotting risk. Screening for clotting disorders is not recommended routinely in pregnancy, but can be considered based on clinical or family history.

Hemodynamic: Blood volume increases during pregnancy to accommodate the pregnancy requirements and increased blood to the placenta. A relative anemia (decreased oxygen carrying capacity by the red blood cells) is common in pregnancy compared to the non-pregnant state. Iron deficiency anemia is also common in pregnancy due to the substantial increase in iron requirement for the growing fetus. The obstetrical care provider may tolerate lower levels oxygen in the blood considered "normal" for pregnancy, but these levels may not be adequate for a pregnant aviator. Finally, the developing baby's blood cells have a higher attraction for oxygen over the mother, also producing a potential relative anemia. These volume, hemoglobin, and anemia-related circumstances can affect a pregnant flyer's G-tolerance, vision, endurance, fatigue, and tolerance for hypoxia (decreased presence of oxygen). Monitoring of the oxygen levels in red blood cells is common in routine prenatal care, but requires additional monitoring for symptoms if flying is considered. The standard replacement of iron and folate in prenatal vitamins is generally adequate, but additional supplementation is often required.

Vaginal Bleeding: Vaginal bleeding can present in all stages of pregnancy, and occurs in up to 25% of all first trimester pregnancies. It can range from minimal to excessive and life-threatening. It can be gradual and painless, or sudden and associated with incapacitating pain. In most cases, small amounts of vaginal bleeding are not associated with dangerous conditions. However, vaginal bleeding can indicate more serious and must always be immediately evaluated. Miscarriages are common events, occurring in 20 to 30% of all recognized pregnancies. Nearly 80% of miscarriages occur in the first trimester. Many miscarriages occur unpredictably without identifiable cause. Because vaginal bleeding occurs frequently in the first trimester, and can lead to unpredictable sudden incapacitation, pregnant aviators are restricted from flight in the first trimester.

Cardiovascular: The base-line heart rate gradually increases throughout a normal pregnancy. The growing uterus exerts pressure on the pelvic veins and the main vein returning blood to the heart that can reduce the amount of blood getting to the heart for each squeeze. Maternal posture can decrease the amount of blood squeezed out with each heartbeat by 25-30%, and some women experience a decrease in blood pressure when lying down leading to possible fainting. The tension within blood vessels are suppressed in the normal pregnancy due to many hormonal changes. During a normal pregnancy, the average blood pressure begins to decrease by 7 weeks of gestation, reaching a low point by 24 to 32 weeks, gradually increasing in the third trimester, and returning to pre-pregnancy levels following delivery. These changes can have significant or subtle effects on the pregnant flyer's cardiac performance, and in turn, can affect G-tolerance, vision, endurance, fatigue, and hypoxia tolerance.

**Pulmonary**: Changes in the lungs can be significant in the aviation environment. There is an increase in maternal oxygen consumption, results in a hyperventilation, lower carbon dioxide levels, and pH changes. The volume of air that the lungs can retain is decreased from physiological changes and uterine enlargement. These changes result in decreased lung functioning. In the flight environment, these can affect hypoxia (decrease in oxygen) tolerance, especially in a situation of rapid decompression during flight.

Renal: In pregnancy, renal (kidney) blood flow and filtering increases by 50%. The increased kidney function and uterine compression of the bladder result in more urine production during a normal pregnancy. This results in more frequent urination, a higher risk of dehydration, and increased potential for kidney stones. The dry flight environment can further induce dehydration.

These factors can have significant or subtle effects on the flyer's G-tolerance, vision, endurance, fatigue, or hypoxia tolerance. Urinary tract infections are more prevalent in pregnancy and must be treated with more vigilance in pregnancy due to the greater risk of kidney infections, and their higher risk of complications.

Gastrointestinal: During normal pregnancies, high circulating levels of progesterone cause decreased activity of the gastrointestinal tract and increased vomiting. Pregnancy-associated vomiting occurs most commonly during the first trimester, but can occur throughout the pregnancy. The vomiting may become frequent enough to require medications to reduce nausea and vomiting. In the rare cases, the episodes become so frequent and severe that intravenous fluid/nutrition is required in addition to anti-nausea medications. Although severe cases of nausea and vomiting are less common, any nausea, vomiting, and retching, can result in significant aeromedical distractions and additional dehydration.

**Endocrinology**: Pregnancy is a state associated with increased insulin circulation, insulin resistance, and a set up for diabetes development. For the mother, this can result in relative increase in circulating blood sugar or frank (gestational) diabetes. In cases of gestational diabetes, control can be achieved with diet and the use of medication reducing blood sugar, although sometimes external insulin is required. Maternal screening for diabetes generally occurs at 26-28 weeks of gestation, but may be performed earlier for risk factors or clinical findings.

**Immune System**: A normal pregnancy has changes that can suppress the immune system. These changes allow the maternal system to tolerate the different immune system of the fetus. As a consequence, a pregnant female can be more susceptible to general infections, and infections can be more severe. More aggressive treatments may be required.

**Ergonomic Considerations**: As the uterus grows during pregnancy, it emerges from the pelvis after 12 weeks and begins to increase abdominal circumference thereafter. Breast tissue enlarges. Size and weight distribution changes can result in requirements for changes within the flight environment or equipment. Localized or generalized swelling can occur in normal pregnancies and may increase the circumference of the arms, legs, and occasionally other areas of the body. Acid reflux up the esophagus is also more common during pregnancy, particularly when lying back. These changes may affect the fit and safety of life support equipment in the aircraft and must be considered initially and throughout the pregnancy.

Sleep: Sleep disturbances during pregnancy are common and can contribute to excess fatigue in the pregnant aviator. These disturbances tend to increase as the pregnancy progresses resulting in additional aeromedical significance.

## **Environmental Effects on the Mother and Fetus:**

Heat exposure: The fetus generates additional heat. The mother is expected to gain 25-35 pounds during the pregnancy. The flight environment and safety equipment may further increase heat exposure to the flyer. The combination of increasing body mass, the flight environment, and fetal heat generation can result in maternal heat intolerance and adverse effects to the fetus. Elevated core body temperature has been shown to double the risk of neural tube defects in the fetus. Animal studies suggest elevated ambient temperatures are associated with an increase in risk of preterm labor and growth restriction. These should be addressed when considering continuation of flight duties in these environmental conditions.

**Sound and Vibration Exposure**: Sound and vibration exposure during the second trimester has been associated with hearing changes identified in the newborn. The hearing organs are developed around 20 weeks gestation and may be susceptible to vibration and noise damage. Significant noise and vibration exposures have been associated with permanent damage to these organs, fetal growth restriction and preterm labor. The maternal abdomen, organs, placenta, and uterus have been shown to provide a modest noise attenuation in animal models. Noise frequencies less than 250 Hz are attenuated less. Limited evidence suggests exposures greater than 115 dBC 8-hour time weighted average (TWA), or 155 dBC pulse, may be associate with fetal hearing effects after 20 weeks gestation. A specific dose effect however, has not been fully elucidated, but reasonable reductions in frequency and duration of exposure can be considered when appropriate.

**Radiation Exposure**: Radiation exposure is a potential risk factor for the fetus, particularly during organ development in the first trimester. Evidence suggests that no adverse fetal effects have been seen with radiation exposures of less than 50 mSv. The average exposure during a 10-hour flight is 0.05 mSv. Population based studies of pregnant commercial airline workers and the associated radiation exposure are reassuring - showing no adverse fetal outcomes, but are not necessarily applicable to military aviation.

Altitude Exposure: A 2014 study suggests that an increase in maternal altitude exposure may be associated with a reduction in birth weight, which increases with increasing altitude exposure. Maternal altitude restrictions are included for flight duty waiver consideration.

Pregnancy-Specific Medical Conditions: Pregnancy-specific conditions can induce a "high-risk" pregnancy that is incompatible with flight duties. It is essential for the obstetrical care provider to perform a complete initial assessment, as well as subsequent assessments to identify these conditions. Prompt notification of the flyer, and her flight surgeon is necessary to identify those conditions incompatible with flying duties. A few examples of pregnancy-specific "high risk" conditions include, but are not limited to: ectopic pregnancy (implantation of the developing embryo outside of the uterus), spontaneous miscarriage, vaginal bleeding, preterm labor, gestational diabetes. Fetal conditions include multiple gestation, birth defects, growth restriction, others. These conditions can be associated with sudden and unexpected pain, bleeding, severe headaches, or even seizure. These can cause life-threatening conditions to the flyer, and significant adverse risk to the pregnancy and fetus. In addition, they can result in subtle or profound distraction or frank incapacitation within the flight environment. Therefore, it is of utmost importance to confirm that a pregnancy is intrauterine, normal, and remains normal throughout any period of continued flight duty.

**Chemical Exposure**: Although somewhat protected by the uterine environment, the fetus is susceptible to the harmful effects of toxic exposures. This risk is greatest in the first 12 weeks of the pregnancy. Animal studies suggest a number of chemicals can cause birth defects and miscarriage, but definitive studies in humans do not exist. Because a number of potentially toxic chemicals are present in the aviation environment, the aviator who flies during pregnancy must consider and minimize this uncertain risk.

**D.** Preexisting Medical Conditions or Medication Use Affected by Pregnancy. There are a variety of medical conditions where the disease, the treatment, or both are affected by pregnancy.

| Such conditions include chronic high blood pressure, elevated blood glucose, diabetes, thyroid disease, inherited blood clotting disorders, migraines, and others. In many cases, a chronic medication or its dose must be changed. Therefore, when an aviator has a preexisting medical condition and/or stable use of a medication previously waived, these must be re-considered prior to returning to flying duties.   |
|--|
| I have read and understand the education within this document. I understand it is not a legal consent form. I have discussed this information with my obstetrician and my flight surgeon. My questions have been answered to my satisfaction. I request permission to continue flying through the 28th week of my pregnancy. I understand I am not required to continue to fly while pregnant and I may voluntarily suspend my participation in aerial flights at any time. I understand that if at any time during the pregnancy, a complication or situation arises making the pregnancy potentially higher risk, I must notify my obstetrician and Flight Surgeon for determination if continued flight status is appropriate. I will comply with all waiver requirements including appointments with my flight surgeon every four weeks (particularly right after OB visits) for the duration of the waiver. |

Printed Name

Signature / Date

#### Dear Doctor,

# Obstetrician Pregnancy Verification for Aviator

Your patient regularly flies on US Air Force aircraft. In order to make a determination as to whether or not she should continue to fly while pregnant, the USAF needs your input.

It is generally accepted that continuing to fly USAF aircraft from the 12<sup>th</sup> through the 28<sup>th</sup> week of gestation in certain specified conditions is safe. However, there is potential for exposure to certain adverse conditions, and some of the physiologic and pathologic states associated with pregnancy may interfere with the patient's ability to perform her job safely. We ask that you discuss these issues with your patient.

Aircraft that are pressured to below (or naturally do not fly above) 10,000 feet, do not contain an ejection seat, and have another qualified pilot on board are potential aircraft for flying while an aviator is pregnant.

While every effort is made to mitigate the risk, there are some adverse conditions that the patient may be exposed to during flight operations. These include:

- Restricted movement for extended periods.
- Oxygen levels in a cabin environment up to 10,000 feet elevation.
- Noise, vibration, radiation, fume exposures
- Sleep disruption/deprivation from shift work

A pregnant aviator is permitted to fly from the 12<sup>th</sup> through the 28<sup>th</sup> week of gestation in the appropriate aircraft provided the following conditions are met:

- The aviator expresses a desire to remain in a flight status while pregnant.
- o The USAF does not require pregnant aviators to continue to fly.
- o Any hesitancy demonstrated by the aviator should result in temporary suspension of flight duties.
- There are no suspected/anticipated pregnancy related complications such as, but not limited to:
- o Any condition which might result in pre-term labor/miscarriage such as multiple gestation
- o Pregnancy induced hypertension, eclampsia/pre-eclampsia
- o Gestational diabetes or glucose intolerance
- o Hyperemesis gravidarum
- o Placenta previa, vasa previa, or incompetent cervix
- o Known or suspected clotting disorders

#### For the Patient:

I have discussed the risks and uncertainties relative to flying while pregnant with my obstetrician. My questions have been answered to my satisfaction. I request permission to fly from the 12<sup>th</sup> through 28<sup>th</sup> week of my pregnancy. I understand I am not required to continue to fly while pregnant and I may voluntarily suspend my participation in aerial flights at any time. I understand that if at any time during the pregnancy, a complication or situation arises making the pregnancy potentially higher risk, I must notify my obstetrician and Flight Surgeon for determination if continued flight status is appropriate.

| Patient Signature / Date | Printed Name |  |
|--------------------------|--------------|--|

| For the Obstetrician:  |  |
|--|--|
| "high risk" pregnancy. I s<br>flights through the 28th w<br>will notify the aviator so | cal or physical conditions related to pregnancy to consider this a support this patient's request to continue participation in aerial week of gestation. If any complications arise during the pregnancy, I she may communicate that with her Flight Surgeon's office. with this pregnancy, or it is considered "high risk," for the |
| If you have any questions about to aviator, please contact her Flight                  | the aviator's flying environment that cannot be answered by the Surgeon's office.  |
| Obstetrician Signature / Date  | Printed Name   |

Your patient works for the US Air Force on the ground, controlling aircraft, or in potentially remote locations controlling missile launches. In order to make a determination as to whether or not she should continue in her current work while pregnant, the USAF needs your input.

Remotely Piloted Aircraft (RPA) Pilots and Sensor Operators, Air Traffic Controllers, and Missile Operators are allowed to continue their duties while pregnant, if the pregnancy is low risk and uncomplicated. Decisions about continued work during pregnancy will be made by these Airmen's Flight Surgeon based off information you provide about their risk and complications.

Obstetrician Pregnancy Verification for Operator

A pregnant operator may be recommended to continue her duties throughout the duration of pregnancy provided there are no suspected/anticipated pregnancy related complications such as, but not limited to:

- o Any condition which might result in pre-term labor/miscarriage such as multiple gestation
- o Pregnancy induced hypertension, eclampsia/pre-eclampsia
- o Gestational diabetes or glucose intolerance
- o Hyperemesis gravidarum
- o Placenta previa, vasa previa, or incompetent cervix
- o Known or suspected clotting disorders

#### For the Patient:

Dear Doctor,

I have discussed my work environment with my obstetrician. My questions about how my pregnancy may affect my ability to do my job have been answered to my satisfaction. I understand that if at any time during the pregnancy, a complication or situation arises making the pregnancy potentially higher risk, I must notify my obstetrician and Flight Surgeon for determination if continued flight or special operational duty status is appropriate.

| 601 |  |
|-----|--|

| Patient Signature / Date  | Printed Name                            |  |  |  |
|---|---|--|--|--|
| For the Obstetrician:  There are no known mental or physical conditions related to pregnancy to const "high risk" pregnancy. I support this patient's request to continue participation work duties. If any complications arise during the pregnancy, I will notify the A may communicate that with her Flight Surgeon's office.  There are complications with this pregnancy, or it is considered "high risk," for |   |  |  |  |
| If you have any questions about the Airman's work env. Airman, please contact her Flight Surgeon's office.  | ironment that cannot be answered by the |  |  |  |

Printed Name

Obstetrician Signature / Date

# PrEP, HIV Pre-Exposure Prophylaxis (Sep 2018)

Reviewed: Dr. Christopher Keirns, Maj Laura Bridge, and Capt Luke Menner (ACS Internal Medicine); Dr. Dan Van Syoc; Lt Col Jason Okulicz (Infectious Disease SG Consultant); and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: Waiver potential for HIV PrEP in USAF aircrew and special duty personnel.

### I. Waiver Consideration

All flying classes, ATC, GBO, and SWA personnel utilizing Truvada® (emtricitabine/tenofovir disoproxil fumarate [FTC/TDF]) for PrEP to reduce the risk of HIV infection require aeromedical waiver. Personnel may be considered for waiver on a case-by-case basis. Waiver will generally be contingent on tolerability of the medication and adherence to the guidelines established by the CDC for HIV PrEP. Clinical follow-up visits are required at least every three months and must include a sexually transmitted infection (STI) symptom assessment, documentation of medication adherence, and behavioral risk reduction counseling to include education and reinforcement of safe sex practices. Additionally, updated HIV testing every three months, bacterial STI testing every three to six months, and serum creatinine (renal function) measurement every six months are required. Discontinuation of HIV PrEP with appropriate counseling about stopping/restarting PrEP is required should the member be TDY/deployed to a location that cannot support continued strict compliance with the CDC guidelines (i.e., any TDY/deployment greater than 90 days). Interval discontinuation of PrEP for the purpose of TDY/deployment followed by resumption upon return to home station does not require new waiver evaluation in the absence of any other clinical changes.

**Table 1: Waiver potential for HIV PrEP** 

| Flying Class (FC) | Waiver<br>Potential <sup>1,2</sup> | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------------------------|------------------|--------------------------|
| FC I/IA           | Yes                                | AFMRA            | No                       |
| FC II/III         | Yes                                | AFMRA            | No                       |
| ATC, GBO, SWA     | Yes                                | AFMRA            | No                       |

- 1. Waiver for both trained and untrained personnel will be considered on a case-by-case basis.
- 2. All required interval quarterly lab work that is obtained following waiver approval will need to be inputted into the "Interim Results" AIMWTS section every 6 months.

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete, the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations. Member must be on the medication for 30 days, have had a 30 day follow up (telephone consult acceptable), before waiver request can be submitted. All required interval quarterly lab work that is obtained following waiver approval will need to be inputted into the "Interim Results" AIMWTS section every 6 months.

## A. Initial Waiver Request:

- 1. Information to include in history:
  - a. Clearly delineate the underlying clinical indications for use of HIV PrEP therapy
  - b. Complete list of current medications with dates of initiation, doses, and all adverse effects
- 2. Consultation reports from all treating providers, which should include:
  - a. At least one clinician visit documenting HIV-negative status
  - b. Assessment for medication side effects
  - c. Discussion of medication tolerance and adherence after beginning PrEP (e.g., one month after initiation)
- 3. Laboratory studies required:
  - a. Recent 4th generation HIV antigen/antibody test
  - b. Baseline serum creatinine
  - c. All other laboratory studies ordered by consulting specialist(s)

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Clearly document member's compliance with required quarterly clinical follow-up and all required laboratory monitoring
  - b. Complete list of current medications with dates of initiation, doses, and all adverse effects
- 2 All interval consultation reports from all treating providers, including all quarterly clinical follow-up notes. Each quarterly clinical follow-up should include the following:
  - a. Description of member's compliance with required clinical and laboratory monitoring
  - b. STI symptom assessment
  - c. Documentation of medication adherence
  - d. Behavioral risk reduction counseling to include education and reinforcement of safe sex practices
- 3 Laboratory studies required:
  - a. All interval measurements of renal function
  - b. All interval HIV test results
  - **c.** All interval bacterial STI testing results

#### III. Aeromedical Concerns

Truvada® (emtricitabine/tenofovir disoproxil fumarate [FTC/TDF]) was FDA-approved in 2012 for HIV pre-exposure prophylaxis (PrEP) in high-risk individuals to mitigate the risk of HIV-transmission. Individuals considered at high-risk of new HIV infection include those with HIV-positive sexual partners; injection drug users who share injection equipment or were in treatment for injection drug use within the preceding six months; and both heterosexual and homosexual individuals engaging in high-risk sexual behaviors as described in CDC practice guidelines for PrEP. Truvada® first gained FDA approval in 2004 for use as a component of combination antiretroviral therapy in individuals with a diagnosis of HIV. TDF and FTC are nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) that inhibit HIV replication and can prevent seroconversion in HIV-negative individuals who are exposed to the virus. The efficacy of

FTC/TDF at reducing the risk of HIV-seroconversion has been demonstrated in multiple studies of high-risk HIV-negative individuals.

TDF/FTC is a well-tolerated medication, and the rate of aeromedically-relevant adverse effects is considered acceptable provided consistent adherence to proper clinical and laboratory monitoring. The most commonly reported adverse effects include gastrointestinal symptoms such as nausea, vomiting, and diarrhea in about 10% of patients and neurologic symptoms such as headache (6%), insomnia (8%), and fatigue (9%). The majority of these symptoms appear to resolve within a month of taking the medication ("start-up syndrome"). There are no reported neurocognitive or neuropsychiatric side effects from FTC/TDF use. The CDC recommends regular laboratory monitoring to assess for HIV-seroconversion, acquirement of other sexually transmitted infections (STIs), and the development of kidney toxicity while on FTC/TDF. Specifically, the CDC recommends HIV testing every three months, bacterial STI testing every three to six months, and serum creatinine (renal function) measurement every six months. Additionally, the CDC recommends clinical follow-up visits with the prescribing provider at least every three months. Each clinical follow-up encounter should include an STI symptom assessment, documentation of medication adherence, and behavioral risk reduction counseling to include education and reinforcement of safe sex practices. The clinical follow-up and laboratory monitoring required while taking FTC/TDF may impose operational and mobility limitations when the frequent monitoring and behavioral counseling are not available. Discontinuation of PrEP by the treatment team for the purpose of extended TDY/deployment (i.e., greater than 90 days) will likely be required.

AIMWTS review prior to Aug 2018 revealed nine aeromedical waiver packages submitted for use of FTC/TDF for HIV PrEP. All cases resulted in disqualification. These cases varied broadly by career field, with three GBC, two FC II, and four FC III waiver requests. Flight and operational experience with FTC/TDF use is limited across all branches of the Department of Defense. FTC/TDF use is disqualifying for all aviator classes in the United States Navy and Army, but aviators taking FTC/TDF are considered potentially eligible for waiver in these services. Two naval aviators carried valid waivers for FTC/TDF use prior to Aug 2018. Four Army officer pilots and two Army enlisted aviators carried valid waivers for FTC/TDF use prior to Aug 2018. The first USAF aeromedical waiver for FTC/TDF use in a FC III aviator was granted in Aug 2018.

| Common ICD-9 codes used for HIV PrEP |                                      |  |  |
|--------------------------------------|--------------------------------------|--|--|
| V01.89                               | Exposure to STD                      |  |  |
| V07.9                                | Other specified prophylactic measure |  |  |
| V69.2                                | High risk sexual behavior            |  |  |

| Common ICD-10 codes used for HIV PrEP |                              |  |
|---------------------------------------|------------------------------|--|
| Z79.899                               | Other long-term drug therapy |  |

#### IV. Suggested Readings

- 1. CDC website: https://www.cdc.gov/hiv/risk/prep/index.html
- 2. Centers for Disease Control and Prevention. Pre-exposure prophylaxis for the prevention of HIV infection in the United States. <a href="https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf">https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf</a>
- 3. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines (2015). Morbidity and Mortality Recommendations and Reports. 2015;64(RR3):1-137.

### WAIVER GUIDE

Updated: Jan 2016

Supersedes Waiver Guide of Jun 2012

By: Lt Col Charles G. Mahakian (RAM 17) and Dr Dan Van Syoc Reviewed by Lt Col Timothy Phillips, AF/SG consultant for Urology

### **CONDITION:**

Prostate Cancer (Jan 2016)

### I. Waiver Consideration.

Prostate cancer, as with all malignancies, is disqualifying for all classes of aviation, as well as for retention.

Table 1. Waiver potential of prostate cancer (assume all cases are adenocarcinoma).

| Flying Class | Condition         | Waiver Potential | ACS review/evaluation |
|--------------|-------------------|------------------|-----------------------|
| (FC)         |                   | Waiver Authority |                       |
| I/IA         | Stages I – IIC    | Yes#†            | Yes                   |
|              |                   | AETC             |                       |
|              |                   |                  |                       |
|              | Stages IIIA – IVB | No               | No                    |
|              |                   | AETC             |                       |
| II/III       | Stages I – IIIB   | Yes+†            | Yes                   |
| ATC/GBO/SWA  |                   | AFMRA            |                       |
|              |                   |                  |                       |
|              | Stages IIIC – IVB | No               | No                    |
|              |                   | AFMRA            |                       |

<sup>#</sup> For untrained personnel, waiver may be considered after 5 years of remission, asymptomatic.

Review of AIMWTS through Jan 2016revealed 97 cases of prostate cancer. Of this total, 0 were FC I/IA, 65 were FC II, 26 FC III, 4 MOD, and 2 ATC. A total of 86 waivers were granted and 11 were disqualified. Of the eleven disqualifications (7 FC II, 3 FC III, and 1 MOD), four were disqualified for medical reasons other than prostate cancer.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for prostate cancer should include the following:

A. History – symptoms, pathology, stage, treatment, including date of last treatment, surveillance plan and activity level.

B. Physical – genital, DRE.

<sup>+</sup> For trained personnel waiver may be considered six months after treatment completed, in remission and asymptomatic.

<sup>†</sup> No indefinite waivers.

- C. Urology/oncology consults to include the six month follow-up all consistent with National Comprehensive Cancer Network (NCCN) guidelines.
- D. Labs All PSA tests with dates.
- E. Pathology report to include Gleason scoring results.
- F. Results of all applicable staging evaluations, including radiology reports.
- G. Tumor board report, military or civilian, if applicable.
- H. Medical evaluation board results.
- I. List any and all treatment for erectile dysfunction or other complication secondary to disease or treatment.

The AMS for <u>waiver renewal</u> for prostate cancer should include the following:

- A. History brief summary of stage, treatment, frequency of surveillance and results, any symptoms, activity level; all must be consistent with NCCN guidelines.
- B. Physical DRE.
- C. Urology/oncology consult.
- D. Labs all PSA test results since previous waiver.
- E. List any and all treatment for erectile dysfunction or other complication secondary to disease or treatment.

### III. Overview.

Prostate cancer is the most common cancer in men, and the second leading cause of cancer death for men, with increasing incidence with age (the median age at diagnosis is 72 and more than 75% of all cases are diagnosed in men older than age 65). It has a tendency to metastasize to bones and lymph nodes. In 2012, the disease was diagnosed in 177,489 men in the United States, and there were 27,244 deaths, with an incidence rate of 105.3 per 100,000 men per year in the US. With the increased utilization of Prostate-Specific Antigen (PSA) screening, the majority of cases are localized at presentation (i.e., not metastatic) and at least 95% of all cases are pathologically classified as adenocarcinoma.

A number of risk factors for prostate cancer have been identified, including increasing age, as noted above. Other factors which confer increased risk for prostate cancer include African-American race and family history. African Americans have the highest incidence of disease and the lowest rates are in men from China and Japan.<sup>5</sup> A positive family history is a risk factor and that risk increases with the number of affected relatives. Diet does appear to play a role in risk as well although not definitively proven as yet. Data does seem to point to an increased risk with consumption of red meat, animal fat, and a higher total fat consumption. Infection and/or inflammation have also been proposed to confer increased risk for prostate cancer, but specific causative organisms have not been identified.<sup>6</sup> For many men, the development of prostate cancer likely results from exposure to multiple environmental factors superimposed on a background of variable genetic susceptibility, making it difficult to identify specific causal events or agents.

The vast majority of cases are found after a routine screening with PSA plus digital rectal exam. PSA does not obviate the need for a digital rectal exam, as some cancers may present with a low PSA but abnormal prostate exam (nodule, induration or asymmetry). Screening with the PSA test has greatly improved detection and most cases are asymptomatic at the time of diagnosis. Symptoms at the time of presentation usually indicate locally advanced or metastatic prostate

cancer. Local symptoms can include dysuria, hematuria, difficulty voiding, frequency, urinary retention, hematospermia or renal colic from ureteral obstruction. Metastatic disease can present with back or hip pain from bone metastases.

One issue is that screening has led to the detection of clinically insignificant prostate cancers that might never progress over a man's lifetime. PSA-based screening has led to an increase in the diagnosis of lower grade, localized prostate cancer.<sup>7</sup> In the United States, 90% of men diagnosed with prostate cancer will seek some form of treatment. With early detection of small tumors, many of these men may incur the side effects of treatment many years before the disease reaches a state where it poses a threat to health or longevity, and as a result may not benefit from early detection. As a result, the U.S. Preventive Services Task Force (USPSTF) recommends against prostate cancer screening, citing that the harms of prostate cancer screening and subsequent treatment outweigh potential benefit in lives saved.

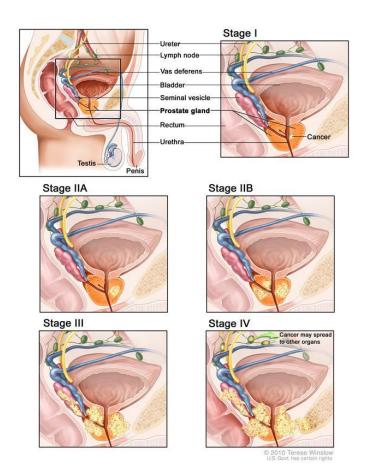
However, the costly problems of over-diagnosis and over-treatment of clinically insignificant prostate cancer must be balanced against incontrovertible public health data that demonstrate a substantial reduction in prostate cancer death with PSA-based screening. The American Urological Association is currently revising its prostate cancer screening guidelines in light of USPSTF recommendations which discourage screening. Their most recent guideline from 2013 recommends against baseline PSA screening between ages 40 to 54 years, in men of average risk. Periodic screening may ensue, but annual screening is no longer recommended for all men, and frequency of screening should be based on baseline PSA and other risk factors. At this time, the American Cancer Society recommends screening with an annual digital rectal exam (DRE) beginning at age 50 for men at average risk and are expected to live at least 10 more years, and recommends earlier screening (age 45) for men at high risk for prostate cancer, which include African American race and first degree relatives diagnosed with prostate cancer before age 65. Men with multiple first degree relatives diagnosed with prostate cancer before age 65 should consider screening as early as age 40.9

If screening with PSA and digital rectal examination indicates an increased risk for prostate cancer, transrectal ultrasound guided (TRUS) biopsy with 10-12 cores (concentrated in the peripheral zone of the gland) is performed for definitive diagnosis.

A PSA of 4 ng/mL is frequently used as the "upper limit of normal", but in actuality there is no level of PSA below which the risk of prostate cancer is negligible. Lower PSA generally indicates lower likelihood of finding prostate cancer on a biopsy. For this reason, men with a lower baseline PSA may consider less frequent screening, although optimal screening intervals have not been validated in large clinical trials. Because benign prostatic hyperplasia (BPH) can also be a source for PSA and because of the increased incidence of BPH as men age, some propose lower thresholds of PSA for recommending biopsy in younger men. In addition, some have identified rate of increase in PSA over time (PSA velocity) as a risk for prostate cancer. These issues make it difficult to identify a "normal cutoff" for PSA. PSA represents a range of risk for prostate cancer, and the risk for prostate cancer should be weighed against a patient's competing risks for morbidity and mortality, such as age, cardiovascular disease, and other serious health conditions.

Table 2. Prostate Cancer Staging Definitions.<sup>13</sup>

|              | te Cancer Staging Definitions. <sup>13</sup>                                  |  |  |
|--------------|---|--|--|
| Stage (cT)   | Clinical Tumor (cT) Stage   |  |  |
| Tx           | Primary tumor cannot be assessed  |  |  |
| T0           | No evidence of primary tumor  |  |  |
| T1           | Clinically inapparent tumor neither palpable nor visible by imaging           |  |  |
| T1a          | Tumor incidental histologic finding in 5 % or less of tissue resected         |  |  |
| T1b          | Tumor incidental histologic finding in more than 5 % of tissue resected       |  |  |
| T1c          | Tumor identified by needle biopsy (e.g., because of elevated PSA)             |  |  |
| T2           | Tumor confined within the prostate  |  |  |
| T2a          | Tumor involves one-half of one lobe or less                                   |  |  |
| T2b          | Tumor involves more than one-half of one lobe but not both lobes              |  |  |
| T2c          | Tumor involving both lobes  |  |  |
| T3           | Tumor extends through the prostate capsule                                    |  |  |
| T3a          | Extracapsular extension (unilateral or bilateral)                             |  |  |
| T3b          | Tumor invades the seminal vesicle(s)  |  |  |
| <b>T4</b>    | Tumor is fixed or invades adjacent structures other than seminal vesicles:    |  |  |
|              | bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall |  |  |
| Stage (pT)   | Pathologic Tumor (pT) Stage   |  |  |
| pT2          | Organ confined  |  |  |
| pT2a         | Unilateral, involving one-half of one lobe or less                            |  |  |
| pT2b         | Unilateral, involving more than one-half of one lobe, but not both lobes      |  |  |
| pT2c         | Bilateral   |  |  |
| pT3          | Extraprostatic extension  |  |  |
| pT3a         | Extraprostatic extension  |  |  |
| pT3b         | Seminal vesicle invasion  |  |  |
| pT4          | Invasion of bladder, rectum   |  |  |
|              | Regional Lymph Nodes - Clinical   |  |  |
| NX           | Regional lymph nodes not assessed   |  |  |
| N0           | No regional lymph nodes metastasis  |  |  |
| N1           | Metastasis in regional lymph node(s)  |  |  |
|              | - Pathologic  |  |  |
| pNX          | Regional nodes not sampled  |  |  |
| pN0          | No positive regional nodes  |  |  |
| pN1          | Metastases in regional node(s)  |  |  |
|              | Distant Metastasis  |  |  |
| M0           | No distant metastasis   |  |  |
| M1           | Distant metastasis present  |  |  |
| M1a          | Non-regional lymph nodes  |  |  |
| M1b          | Bone(s)   |  |  |
| M1c          | Other site(s) with or without bone disease                                    |  |  |
|              | Histological Grade Scoring (Gleason)  |  |  |
| Gleason X    | Grade cannot be assessed  |  |  |
| Gleason ≤ 6  | Well differentiated (slight anaplasia)  |  |  |
| Gleason 7    | Moderately differentiated (moderate anaplasia)                                |  |  |
| Gleason 8-10 | Poorly differentiated/undifferentiated (marked anaplasia)                     |  |  |
|              | 1 \   |  |  |



Staging (an estimation of the extent of the tumor) is based on the clinical exam and biopsy findings. If metastatic disease is suspected, additional studies such as CT, MRI or bone scans can be performed, but are not frequently indicated in patients presenting with localized disease. Radiolabeled monoclonal antibody scanning (Prostascint) or PET scanning with 11C-Acetate or 11C-Choline have been used for prostate cancer staging, but both modalities have significant limitations due to poor specificity and sensitivity. Prostate adenocarcinoma is graded, using the Gleason grading or scoring system. Gleason grading is based on glandular architecture and a score ranging from 2 to 10 is assigned. A score of 2 to 6 indicates a well differentiated tumor, a score of 7 indicates a moderately differentiated tumor, and a score of 8-10 indicates a poorly differentiated tumor. Although tumors with a score of 7 have traditionally been grouped with moderately differentiated tumor, a Gleason score of 7 is associated with increased risk for disease progression and cancer-specific mortality compared to a score of 6 or less. 14, 15

Patients can be grouped into risk strata or categories according to the 2009 American Joint Committee on Cancer AJCC Anatomic Stage/Prognostic Group, which is based on tumor size, Gleason score, PSA level, the presence or absence of spread to regional lymph nodes, and the presence or absence of distant metastases. <sup>16</sup> These risk categories correlate with increasing risk of PSA failure and prostate cancer-specific mortality following radical prostatectomy, external beam radiotherapy, or interstitial prostate brachytherapy. <sup>14, 17</sup>

Table 3. Anatomic Stage/Prognostic Groups. 13

| Stage | Primary   | Regional    | Regional Distant Prostate- Hist |               | Histologic Grade |
|-------|-----------|-------------|---------------------------------|---------------|------------------|
|       | Tumor (T) | Lymph Nodes | Metastasis                      | Specific      | (Gleason)        |
|       |           | (N)         | (M)                             | Antigen (PSA) |                  |
| I     | T1a-c     | N0          | M0                              | PSA <10       | Gleason ≤6       |
|       | T2a       | N0          | M0                              | PSA <10       | Gleason ≤6       |
|       | T1-2a     | N0          | M0                              | PSA X         | Gleason X        |
| IIA   | T1a-c     | N0          | M0                              | PSA <20       | Gleason 7        |
|       | T1a-c     | N0          | M0                              | PSA ≥10<20    | Gleason ≤6       |
|       | T2a       | N0          | M0                              | PSA ≥10<20    | Gleason ≤6       |
|       | T2a       | N0          | M0                              | PSA <20       | Gleason 7        |
|       | T2b       | N0          | M0                              | PSA<20        | Gleason ≤7       |
|       | T2b       | N0          | M0                              | PSA X         | Gleason X        |
| IIB   | T2c       | N0          | M0                              | Any PSA       | Any Gleason      |
|       | T1-2      | N0          | M0                              | PSA ≥20       | Any Gleason      |
|       | T1-2      | N0          | M0                              | Any PSA       | Gleason ≥8       |
| III   | T3a-b     | N0          | M0                              | Any PSA       | Any Gleason      |
| IV    | T4        | N0          | M0                              | Any PSA       | Any Gleason      |
|       | Any T     | N1          | M0                              | Any PSA       | Any Gleason      |
| 1     | Any T     | Any N       | M1                              | Any PSA       | Any Gleason      |

For men with prostate cancer clinically confined to the gland, risk is defined as:

- •Very low risk T1c, Gleason score  $\leq$ 6, PSA <10 ng/mL, fewer than 3 prostate biopsy cores positive,  $\leq$ 50 % cancer in any core, or PSA density <0.15 ng/mL/g.
- •Low-risk disease T1-T2a, Gleason score ≤6, PSA <10 ng/mL.
- •Intermediate-risk T2b-T2c, Gleason score 7, or PSA 10-20 ng/mL.
- •High-risk T3a, Gleason score 8-10, or PSA >20 ng/mL.
- •Very high-risk T3b-T4, primary Gleason pattern 5, or >4 cores with Gleason score 8 to 10
- •Metastatic Any T, N1.<sup>16</sup>

The decision whether or not to treat prostate cancer and the choice of treatment should depend on a man's expected longevity, comorbidities, and genitourinary health status (such as erectile function, fertility concerns, symptoms of BPH), in conjunction with the clinical characteristics of his cancer (symptoms, stage, grade, PSA, risk category). Currently, high level evidence to support one form of treatment over others is lacking, and the decision should be individualized, based on above factors. Treatment options for localized prostate cancer include active surveillance, radical prostatectomy (RP), external beam radiotherapy (EBRT), and brachytherapy. Practice guidelines for the management of localized prostate cancer have been developed by the American Urological Association and can be found at <a href="https://www.AUAnet.org">www.AUAnet.org</a>.

Patients falling into a low risk category may do well with any of the above options, as monotherapy. Intermediate risk tumors have an increased risk for progression, and therefore may not be good candidates for active surveillance in men with expected longevity of 10 or more years. Patients with high risk disease are very likely to progress and therefore are not good candidates for active surveillance unless they have significant competing risks for mortality in the short term. In

addition, both intermediate and high risk tumors are more likely to require more than one mode of therapy for disease control, and more likely to recur and progress despite therapy. Combination therapy (i.e. radiotherapy + androgen deprivation) appears to afford better disease control for intermediate and high risk disease compared to monotherapy.

When metastatic disease is likely or definitively diagnosed, the first line treatment is androgen deprivation therapy (ADT). This can be accomplished with surgical castration, or with depot injections or implants of LHRH agonists. ADT is the primary therapeutic approach for men with metastatic disease, alleviating bone pain in 80 to 90 percent of men and leading to objective responses in the serum PSA, and it may modestly prolong survival. Other options for advanced disease or failure of previous therapies include RT (if previous therapy was surgery), RP in a small well-selected group of men with previous RT, and cryotherapy. Systemic chemotherapy (docetaxel and cabazitaxel) is used to treat metastatic prostate cancer that has progressed despite androgen deprivation therapy. Recently, sipuleucel-T (Provenge), an immunotherapy, was approved for treatment of castration-resistant prostate cancer.

The choice of therapy is based on stage of the disease, patient age, any co-morbid conditions, concern about treatment side effects on the quality of life (QOL), and ultimately, the patient's desires. As with any cancer treatment, the goals are to prevent death and disability and to minimize the complications of the therapy. Goals need to be very clear to all involved (patient, family and treatment team). As prostate cancer is a disease of older men, life expectancy (is there a reasonable chance that the man will be alive in ten years?), rather than patient age, should be a major factor in the selection of treatment for a given man. Other factors are overall health status, and tumor characteristics. Currently, there are no evidence-based recommendations for when to intervene in patients with a long life expectancy since markers of disease progression are poorly validated. <sup>16, 19</sup>

Radical prostatectomy (RP) has been used to treat prostate cancer for many years. It can be performed by a retropubic or perineal approach, laparoscopically, and with robotic assistance. In 2008, the majority of treated men chose radical prostatectomy (this is also true in our Air Force population). Life-threatening complications to this procedure are very rare, but there are complications that are common and can be troublesome to the patient. Urinary incontinence, due to damage to the urinary sphincter, can occur and is more common in older men, but normally diminishes with time. Impotence, or erectile dysfunction (ED), can result due to damage to the cavernosal nerves. Nerve-sparing can be performed for clinically localized prostate cancer, with 2/3 to 3/4 of men recovering erectile function if they have good pre-surgical function and if bilateral nerve sparing can be performed.

The two forms of RT available to treat prostatic cancer are EBRT and interstitial implantation, also known as brachytherapy. ERBT is administered daily for 7-8 weeks, and is usually photon therapy. Proton therapy can also be used in conjunction with photon therapy, but is not widely available and evidence is lacking to demonstrate superiority of proton therapy in terms of both cancer control and treatment morbidity. Prospective trials investigating higher dose fractionation are underway to determine if a tumoricidal dose can be delivered over a shorter time frame with acceptable toxicity and cancer control. Brachytherapy involves placing radioactive, rice-sized pellets directly into the prostate gland, in a same-day outpatient procedure. The advantages to this approach over EBRT are convenience and better preservation of sexual function. Brachytherapy results in negligible radiation exposure to medical personnel and family members.<sup>17</sup> Sexual dysfunction is very

common after EBRT, but is better preserved with brachytherapy. Urinary incontinence is not as common as with RP, but irritable bowel and bladder complaints can occur.<sup>7</sup>

Patients with low risk disease or significant competing risks for mortality may be candidates for active surveillance. Unfortunately, a standardized, ideal follow-up regimen supported by high level evidence does not yet exist. Active surveillance regimens are currently being evaluated in several prospective trials, but due to the long natural history of prostate cancer, it may be quite some time before the optimal candidates for active surveillance and the optimal regimen of surveillance are identified. Current regimens include periodic PSA, digital rectal exams and repeat biopsies, but it is not known whether these are sufficient to identify incipient progression before it is too late to successfully intervene. Advantages of active surveillance include (1) avoiding some of the more troublesome side effects of treatment, (2) maintenance of quality of life and daily activities, (3) avoidance of unnecessary treatment of low-grade tumors, and (4) decreased initial costs.<sup>7</sup> It is unknown whether patients managed with active surveillance will have cancer-specific survival comparable to those managed with early intervention.

The largest randomized prospective trial to date investigating early treatment with prostatectomy vs. no treatment (watchful waiting) in men with localized prostate cancer recently published 10-year follow up data. Investigators identified significantly reduced disease specific mortality and reduced risk of metastatic disease among men randomized to radical prostatectomy, compared to those with no treatment. Interim reports at 5 and 8 years identified a cancer-specific and overall mortality advantage to prostatectomy over watchful waiting. Overall mortality at 10 years, however, was not significantly different. It would seem, then, that the prostate cancer intervention allowed men to live long enough to die from other causes, and reinforces the common practice of deferring definitive local therapy for men not expected to live 10 or more years. Two positive predictors for survival in those randomized to no initial treatment were a Gleason score less than 7 and a PSA level less than or equal to 10 ng/mL at the time of diagnosis, i.e. men with favorable risk disease. It would appear that younger patients electing no treatment have a significant probability of progression from localized and indolent to metastatic mortal disease after long-term follow-up. Due to the age of most Air Force aviators with the disease, active surveillance would be an unlikely treatment choice.

At this time, there is little high-quality evidence to guide physicians, patients, and families to formulate the best treatment plan, especially in men with PSA-detected disease. The very few randomized controlled studies are either inconclusive or have not reached maturity in order to give more definitive guidance.<sup>15</sup> All treatments (including no treatment) can cause adverse events and the severity varies among treatments.<sup>23</sup>

For patients with metastatic or locally advanced disease (stages III and IV), more aggressive options need to be considered after the standard three (RP, RT, and active surveillance).

One of the more important considerations in the care of men with prostate cancer is appropriate follow-up care. There are no clearly-defined criteria to prompt therapy in those undergoing active surveillance or to signal recurrence in those who have undergone some form of definitive therapy. Some of the widely used strategies include: a significant increase in serum PSA or a decrease in PSA doubling time to three years or less; a change in the DRE; or a detection of disease progression on surveillance biopsies. For the majority of men in our aviation population who undergo RP and

are pathologic stage T2 with negative surgical margins, with a Gleason score of six or less, the follow-up should consist of a PSA at three months post-operatively, and then every six months for four years and then annually. If the Gleason score is seven or greater, there are positive surgical margins, or pathologic stage is >T2, the testing should be every three months for two years, then every six months for an additional two years, followed by annual testing thereafter.<sup>24</sup> Those men on active surveillance and not electing RP or other primary treatment modality should have a new biopsy annually for the first several years to confirm lack of disease progression. If there is a concern about possible metastasis, an initial or repeat bone scan is in order to rule out bone metastasis.

#### IV. Aeromedical Concerns.

The aeromedical concerns for most men are based more on the treatment and possible complications than on the disease itself. If the aviator is off all treatment medications and is disease-free (considered to be in remission) and asymptomatic, he can be considered for a waiver.

| ICD-9 Codes for Prostate Cancer |                                   |
|---------------------------------|-----------------------------------|
| 185                             | Malignant neoplasm of prostate    |
| 233.4                           | Carcinoma in situ of the prostate |

| ICD-10 Codes for Prostate Cancer |                                   |
|----------------------------------|-----------------------------------|
| C61                              | Malignant neoplasm of prostate    |
| D07.5                            | Carcinoma in situ of the prostate |

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#### WAIVER GUIDE

Updated: Jun 2017

Supersedes Waiver Guide of Feb 2014

By: Lt Col Eric M. Chumbley (RAM 17) and Dr Dan Van Syoc Reviewed by Col Timothy Phillips, AF/SG consultant for urology

### **CONDITION:**

Prostatic Hyperplasia, Benign (Jun 2017)

#### I. Waiver Consideration.

Symptomatic Benign prostatic hyperplasia (BPH) with urinary retention is disqualifying for FC I/IA, FC II, FC III, and SWA duties.. Asymptomatic BPH, and history of invasive surgical therapy such as TURP are not disqualifying, and do not require waiver submission if the obstructive symptoms are relieved, urinary continence is maintained, and healing is complete; in addition, any complications from surgery would be disqualifying.. Of note, it is recommended that after invasive surgery, the aviator remain DNIF for a minimum of 3 weeks to heal due to the risk for acute bleeding and post-operative urgency. Furthermore, DNIF is required if the patient's symptoms remain operationally significant, regardless of the treatment course. BPH is not disqualifying for retention or for ATC or GBO personnel, but certain medications used to treat symptomatic BPH may require waiver.

**Table 1: Waiver potential for Benign Prostatic Hyperplasia** 

| Flying Class (FC) | Waiver Potential | Review/Evaluation at the |
|-------------------|------------------|--------------------------|
|                   | Waiver Authority | ACS                      |
| I/IA              | Maybe*#          | No                       |
|                   | AETC             |                          |
| II, III           | Yes*+\$          | No                       |
| SWA               | MAJCOM           |                          |
| ATC and GBO       | N/A!             | N/A                      |

<sup>\*</sup>No indefinite waivers

AIMWTS review in Jun 2017 revealed 164 cases submitted with a diagnosis of BPH. Of the total, there was 1 FC I/IA case, 92 FC II, 55 FC III, 3 ATC/GBC, 11 MOD, and 2 RPA pilot cases. There were 19 disqualifications, however only 7 in which BPH was a principal disqualifying diagnosis (usually for BPH treated with alpha blockers). Of the 7 disqualifications, four were FC II (3 pilots and 1 flight surgeon) and 3 were FC III.

<sup>#</sup> This problem is very unlikely in the predominately young population contemplating flying training. Such a case will need to be worked up very carefully to rule out other sources of GU pathology.

<sup>+</sup> No waiver required if symptoms are mild (less than seven on the AUA-SI Scale) without evidence of urinary retention and watchful waiting is the "treatment".

<sup>\$</sup> If treated with an approved alpha-blocker, waiver should be restricted to non-high performance aircraft. Pilots on alfuzosin and tamsulosin should also be restricted to flying with another qualified pilot, e.g., FC IIC (non-high performance, with another qualified pilot). Pilots on silodosin are eligible for FC IIA waiver (see "Aeromedical Concerns" above).

<sup>!</sup> BPH is not disqualifying for ATC or GBO personnel, but certain medications used to treat symptomatic BPH may require waiver.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for benign prostatic hyperplasia should include the following:

- A. Complete symptom history to include sensations of incomplete emptying of the bladder, urinary frequency, stopping and starting of urinary stream, urinary urgency, weak stream, difficulty initiating stream and nocturia. Discuss all attempted treatments/medications to include results and side effects.
- B. AUA-SI score.
- C. List and fully discuss all clinical diagnoses requiring a waiver.
- D. Exam: GU exam to include a digital rectal exam.
- E. Laboratory: urinalysis, PSA, urine flow rate, and post-void residual. Some cases may require a more detailed evaluation to include cystoscopy, 24-hour urine for creatinine clearance and protein, IVP, renal/prostate ultrasound, and serum creatinine.
- F. Consult: Urology evaluation if surgery performed or symptoms severe, otherwise, a report from the treating physician will suffice if treated medically.

The following information will be required for <u>waiver renewal</u> every three years (if any abnormalities surface in the interim, they will need to be addressed appropriately). Each item should highlight any evidence for or against progression from earlier assessments:

- A. Interim history to include change in symptoms, medication usage, and side effects.
- B. AUA-SI Score with prior year(s) comparison.
- C. Exam: digital rectal exam and any other pertinent exam findings.
- D. Serum PSA with prior year(s) comparisons.
- E. Current treatment doses and documentation of therapeutic benefit.
- F. Report from treating physician.

### III. Overview.

BPH, one of the most common diseases of aging men, can be associated with bothersome lower urinary tract symptoms (LUTS) that include increased urinary frequency, nocturia, hesitancy, urgency and a weak urinary stream. Chronic inability to completely empty the bladder may cause bladder distention with hypertrophy and instability of the detrusor muscle. BPH can affect quality of life by interfering with normal daily activities and sleep patterns. The prevalence of histopathologic BPH is age-dependent, with initial development usually after age 40. By age 60, its prevalence is greater than 50% and by age 85 it is as high as 90%. Similar to that of histologic evidence, the prevalence of bothersome symptoms also increases with age. Approximately one half of all men who have a histologic diagnosis have moderate to severe LUTS. Determining prevalence of BPH across different populations groups is problematic due, at least in part, to lack of a common definition. Nevertheless, some studies have indicated a lower prevalence of BPH among Asians compared to blacks or whites. Despite similar prevalence, black men are more likely than white men to have more severe LUTS.

Causally, there is growing interest in the relationship of inflammation and BPH. In fact, inflammation of the prostate appears to be more closely related to BPH than chronic prostatitis. Indeed, it is postulated that inflammation actually mediates an association between BPH and obesity, which has been identified as a risk factor for BPH. Recent work has also found a link between both chronic inflammation and the endocrine changes associated with BPH and abnormal stem cell expansion. The question is whether inflammation and endocrine changes disturb and damage prostate tissue, or if abnormal stem cell changes cause inflammation and endocrine changes. If it ultimately appears that inflammation initiates the cycle that ultimately leads to BPH, we may see treatment of BPH with therapies that target inflammation. But at this time, there is insufficient evidence to support the treatment of BPH with antibiotics or anti-inflammatory medications, such as NSAIDs.

Because long-term data from population-based studies have only recently become available, the risks of developing complications and morbidities from untreated BPH are unclear. For example, despite recent evidence, there is still uncertainty regarding the likelihood that a patient with a specific symptom complex will develop acute urinary retention within a particular time frame. Nonetheless, BPH-associated mortality is rare in the United States, and serious complications are uncommon. In contrast, LUTS are bothersome to many patients, and the degree of complaint varies greatly among individuals with the same symptom frequency and severity. Since the impact of LUTS on the patient's quality of life is highly variable and not directly related to measurable physiological factors, the patient's perception of the severity of the condition, as well as the degree to which it interferes with his lifestyle, should be primary considerations in choosing therapy. Large-scale studies of different populations have demonstrated consistent evidence of a relationship between LUTS symptoms and ejaculatory dysfunction that is independent of age and other comorbidities. In the patient of the severity dysfunction that is independent of age and other comorbidities.

BPH has been defined as prostate enlargement from progressive hyperplasia of stromal and glandular prostatic cells, and clinically as LUTS associated with benign prostatic enlargement (BPE) causing bladder outlet obstruction (BOO).<sup>5</sup> The diagnosis of BPH is made by a combination of history (see above), physical examination (symmetrically enlarged prostate without asymmetry or nodularity on digital rectal exam), and laboratory tests (esp. urinalysis and prostate specific antigen or PSA). An American Urological Association Symptom Index (AUA-SI) (see Table 2) of > 7 AUA-SI and a peak urinary flow rate < 15 mL/s are also suggestive of BPH. However, the greatest value of the AUA-SI is not in making the diagnosis of BPH, but in assessing the severity of symptoms and their progression. Other diagnoses that should be considered with this clinical presentation include urethral stricture, bladder neck contracture, carcinoma of the prostate or bladder, bladder calculi, urinary tract infection, prostatitis, and neurogenic bladder.<sup>2</sup>

Table 2 - AUA Urinary Symptom Index (AUA-SI)<sup>3</sup>

| Questions to be Answered   | Not at all | Less<br>than 1<br>time in<br>5 | Less<br>than<br>half<br>the<br>time | About<br>half<br>the<br>time | More than half the time | Almost<br>always    |
|--|------------|--------------------------------|-------------------------------------|------------------------------|-------------------------|---------------------|
|  |            | Circle or                      | ne numbe                            | er for eacl                  | n question              |                     |
| 1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?                                 | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?  | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 3. Over the past month, how often have you found you stopped and started again several times when you urinated?  | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 4. Over the past month, how often have you found it difficult to postpone urination?   | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 5. Over the past month, how often have you had a weak urinary stream?  | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 6. Over the past month, how often have you had to push or strain to begin urination?   | 0          | 1                              | 2                                   | 3                            | 4                       | 5                   |
| 7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning? | 0 (none)   | 1 (1 time)                     | 2<br>(2<br>times)                   | 3 (3 times)                  | 4 (4 times)             | 5 (5 or more times) |
| Sum of circled numbers (AUA symptom  | score):    |                                |                                     |                              |                         |                     |
| 0 to 7: Mild symptoms  |            |                                |                                     |                              |                         |                     |
| 8 to 19: Moderate symptoms 20 to 35: Severe symptoms   |            |                                |                                     |                              |                         |                     |

For all men presenting with LUTS, the AUA recommends the following:

- 1. Relevant medical history.
- 2. Assessment of LUTS, including determining severity and symptom bother with AUA-SI.
- 3. Physical examination with DRE.
- 4. Urinalysis (helps rule out other conditions).
- 5. Serum PSA (tends to correlate with prostate volume; may also point to prostate cancer).

<u>Note</u>: urine cytology should also be obtained in men at risk of bladder cancer, particularly if they have associated urinary frequency and urgency or hematuria.<sup>1, 2</sup>

Treatment options for BPH include watchful waiting, medications and surgery. The decision to treat involves balancing the severity of the patient's symptoms with potential side effects of therapy.

Watchful waiting is recommended in men who have mild symptoms (AUA-SI of less than 7) or who do not perceive their symptoms to be particularly bothersome. These men should be monitored at least annually for symptom progression.<sup>1</sup> For those whose symptoms are more bothersome, further evaluation is warranted with a Frequency-Volume Chart to establish polyuria and the degree of nocturia. The AUA has published a Clinical Practice Guideline (CPG), which contains helpful treatment guidance.<sup>2</sup>

When selecting a pharmacologic agent, the treating physician needs to take into consideration the nature of the patient's disease, side effects of the selected agent and the potential for drug interactions with other medications in use. The BOO of BPH involves both a dynamic and a structural pathophysiologic component. The dynamic (physiologic, reversible) component is related to the tension of prostatic smooth muscle in the prostate, prostate capsule, and bladder neck. The fixed (structural) component is related to the bulk of the enlarged prostate impinging on the urethra. Alpha-adrenergic antagonists and 5-alpha-reductase inhibitors act upon the dynamic and fixed components, respectively. Alpha-adrenergic antagonists (terazosin, doxazosin, tamsulosin, alfuzosin, and prazosin) appear to be more effective for short-term treatment of symptoms but do not appear to have an impact on reducing long-term complications, such as urinary retention or the need for surgical intervention. Only 5-alpha-reductase inhibitors (finasteride and dutasteride) have demonstrated the potential for long-term reduction in prostate volume, which in turn reduces the long term risks of urinary retention and surgical intervention. Regarding erectile dysfunction, the alpha-adrenergic antagonists appear to have a lower incidence of this potential side effect than do the 5-alpha-reductase inhibitors.<sup>11</sup>

There is increased interest in "natural" remedies for BPH. The most popular such agent over the past few years has been saw palmetto, an extract of the berry by that name. In 2001 an estimated 2.5 million adult Americans used this product. A recent trial compared saw palmetto with placebo and found that there was no difference after one year in the two groups in AUA-SI scores, maximal urinary flow rates, prostate size, residual volume after voiding, quality of life, or PSA scores. This study and others examining the efficacy of dietary supplement-like substances (including beta-sitosterol) raises questions about the variability of botanical products as well as their overall efficacy compared to their claims. Complementary and alternative treatments of BPH including the "natural" remedies above and acupuncture are not recommended.

Historically, the most commonly performed surgical treatment for BPH is transurethral resection of the prostate (TURP). Post-operatively, the patient is left with a wide open prostatic fossa bound by a denuded surgical capsule that will be lined by a newly regenerated epithelial surface in 6 to 12 weeks. Until this occurs, the patient is vulnerable to bleeding and most surgeons encourage avoidance of straining for at least six weeks. Most men note a marked decrease in symptom scores and a substantial increase in maximal urinary flow rates post-operatively. Side effects to this procedure include bleeding, incontinence and urethral strictures, all relatively uncommon. Most men will experience retrograde ejaculation after this procedure. Newer surgical options include several procedures with lasers, transurethral incision of the prostate, electrovaporization of prostate tissue, as well as several minimally invasive procedures such as transurethral needle ablation of the prostate and microwave thermotherapy. These have demonstrated efficacy as well, but are not appropriate for all TURP candidates. Urethral stents have been studied for BPH indications and are available, but have been abandoned by most urologists due to the tendency for tissue growth through stent fenestrations and encrustation of stent material.

# IV. Aeromedical Concerns.

The presence of BPH symptoms alone is not automatically disqualifying for flying duties. The primary aeromedical and operational concern with BPH relates to the potential for urinary obstruction/retention. The symptoms of acute urinary retention include severe lower abdominal pain, a distended abdomen, and the sudden inability to pass urine. Operationally, urinary frequency can be disruptive, and nocturia can result in sleep disruption and fatigue. The tendency to delay bladder emptying while in-flight can lead to excessive bladder distention and acute urinary retention. As such, judgment should be used in determining the aeromedical significance of reported symptoms.

Medical therapy for BPH should also be assessed for the possibility of aeromedically significant side effects. Regarding the 5-alpha-reductase inhibitors, specifically finasteride, a detailed aeromedical medication review in Sep 04 concluded it to be both effective and safe in the aerospace environment. More recently, three alpha-1-adrenergic antagonists (silodosin, tamsulosin, and alfuzosin) were reviewed for use in flyers. These medications were approved for aviator use but restricted to non-high performance aircraft due to the risk of orthostasis. Pilots are *also* restricted to flying with another qualified pilot if tamsulosin or alfuzosin is used. Silodosin does *not* require the latter restriction for pilots since it has a more favorable cardiac side effect profile due to its exceptional alpha-1 subtype selectivity. Surgical treatment for BPH should result in grounding for several weeks, with a return to flying as long as the symptoms are relieved with the procedure. Furthermore, "natural" products such as saw palmetto and beta-sitosterol should be considered cautiously, with the knowledge and approval of the flight surgeon, due to significant questions regarding efficacy, side effect profile, and the lack of regulation regarding contents and purity of these over-the-counter supplements.

| ICD-9 code for Benign Prostatic Hyperplasia |                         |
|---|-------------------------|
| 600   | Hyperplasia of prostate |

| ICD-10 code for Benign Prostatic Hyperplasia |                   |
|--|-------------------|
| N40  | Enlarged prostate |

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## Prostatitis (Jun 2019)

Reviewed: Maj Andrew Long (RAM 20), Dr. Dan Van Syoc (ACS Waiver Guide coordinator), Lt Col Christopher Allam (AF/SG Urology consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Format

#### I. Waiver Consideration

Acute prostatitis, National Institute of Health Classification I (NIH I) symptoms are not compatible with flying duties and require DNIF. Chronic prostatitis (NIH II – IV) and abscess of the prostate are disqualifying for all flying classes including Special Warfare Airmen (SWA). Prostatitis is not disqualifying for ATC/GBO personnel, nor is it disqualifying for retention purposes IAW the MSD (13 May 2019, J48).

**Table 1: Waiver potential for Prostatitis** 

| Flying Class | Condition <sup>5</sup> | Waiver Authority             | ACS Review/ |
|--------------|------------------------|------------------------------|-------------|
| (FC)         | Condition              | Waiver Potential             | Evaluation  |
| I/IA         | NIH I                  | N/A                          |             |
|              | NIH II                 | No <sup>1</sup>              |             |
|              |                        | AETC                         |             |
|              | NIH III                | $No^2$                       | No          |
|              |                        | AETC                         |             |
|              | NIH IV                 | No <sup>3</sup>              |             |
|              |                        | AETC                         |             |
| II/III       | NIH I                  | N/A                          |             |
| SWA          | NIH II                 | Yes                          |             |
|              |                        | MAJCOM                       |             |
|              |                        | 2.5                          | No          |
|              | NIH III                | Maybe <sup>2, 4</sup> MAJCOM |             |
|              |                        | WIAJCOWI                     |             |
|              | NIH IV                 | Maybe <sup>3</sup>           |             |
|              |                        | MAJCOM                       |             |
| ATC/GBO      | Prostatitis            | N/A                          | N/A         |

<sup>1.</sup> Risk of recurrent and prolonged infections prevents waiver for I/IA.

<sup>2.</sup> Treatment of chronic pain is usually with alpha-blockers and they are not waivered for FC I/IA or II and are rarely waivered for FC III (alpha blocker's aeromedically significant side effects include postural hypotension, dizziness, vertigo and syncope).

<sup>3.</sup> Responsive conditions like prostate cancer may be waived for trained FC II or III once treatment completed and six months has elapsed. See prostate cancer waiver guide.

<sup>4.</sup> Waiver for untrained personnel is unlikely.

<sup>5.</sup> See section III below for discussion of disease categories

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

# A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. Document current absence of symptoms and any medication side effects.
  - b. Document return to full physical activity or specify activity limitations
- 2. Complete exam: general exam with temperature, external urologic exam and rectal exam.
- 3. Urinalysis, cultures and labs such as PSA and CBC if required.
- 4. Urologist's consultation, diagnosis and study results to rule out other abnormalities, including follow-up notes after acute resolution. (Consultation notes and test results should be scanned into AIMWTS.)
- 5. In NIH III/CPPS cases, consider the psychological status of the flyer.
- 6. Any other pertinent information.
- 7. The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Summary of recurrence frequency, symptoms, treatment with any side effects and activity levels.
- 2 External urologic exam and rectal exam.
- 3 Urology consultation.
- 4 Any other pertinent information.
- 5 The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.
- 6 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Prostatitis, or increased inflammatory cells within the prostatic parenchyma, is classified into four categories by the National Institutes of Health (NIH) discussed below. Initial diagnosis is made by history, physical, urinalysis and cultures. Urinalysis and cultures may be obtained before and after prostatic massage in NIH categories II – IV. However, prostatic massage should be avoided in acute prostatitis or during acute illness due to the risk of inducing bacteremia. The recurrent infections or inflammations seen in NIH II – IV require urology consultation, but acute prostatitis does not unless complicated by abscess. Primary aeromedical concerns of prostatitis involve recurrent distracting symptoms, medication side effects, and vibration and G-load forces that may exacerbate prostatitis.

- 1. Acute bacterial prostatitis (NIH I). Symptoms include fever, genitourinary pain (suprapubic, perineal or rectal), obstructive voiding symptoms, dysuria, urgency, frequency, malaise, nausea and vomiting and can progress to frank septicemia. Approximately 5% of these patients will progress to a type of chronic prostatitis. These distracting symptoms are not compatible with flying duties and require DNIF until asymptomatic.
- 2. Chronic bacterial prostatitis (NIH II). Typically affects men aged 40-70 years with histories of recurrent UTIs, often predisposed by an inadequately treated initial acute infection or functional voiding abnormalities. Members are often asymptomatic between recurrences but bacteriuria persists. Identifiable uropathogens are present in less than 5% of these patients. The likelihood of recurrent rapid onset of distracting symptoms makes this condition incompatible with flying duties unless cured or suppressed with antibiotics.
  - a. Chronic pelvic pain syndrome (CPPS) (NIH III). Most cases of prostatitis in the general population involve this category of chronic genitourinary pain without uropathogenic bacteria. Members have many symptoms of traditional prostatitis but also report pain in the perineum, suprapubic area, penis, groin or lower back, and may report pain during or after ejaculation. Over 50% of patients may experience painful ejaculation. There are two subtypes distinguished by the degree of white blood cells (WBCs) in prostatic secretions, urine or semen but the clinical utility of this academic distinction is questioned:Nonbacterial prostatitis or inflammatory CPPS (NIH IIIA).
  - b. Prostatodynia or noninflammatory CPPS (NIH IIIB).
- 3. <u>Asymptomatic inflammatory prostatitis (NIH IV).</u> WBCs are seen in prostatic secretions, post-prostatic massage urine, semen or histological sections of the prostate but the patient is completely asymptomatic. No infection is present and cultures are negative. These patients may have elevated PSA, benign prostatic hypertrophy, or prostate cancer. Full urological workup is required for waiver submission to better assess the aeromedical risk.

AIMWTS review in Jun 2019 showed waiver submissions for 26 cases of prostatitis Jan 2014. Breakdown of the cases: 16 FCII and 10 FCIII. Only one case (FC III) was disqualified.

| ICD-9 codes for Prostatitis |   |  |
|-----------------------------|---|--|
| 601.0                       | Acute prostatitis                                     |  |
| 601.1                       | Chronic prostatitis                                   |  |
| 601.2                       | Chronic prostatitis                                   |  |
| 601.4                       | Prostatitis in disease classified elsewhere           |  |
| 601.8                       | Other specified inflammatory diseases of the prostate |  |
| 098.12                      | Gonococcal prostatitis (acute)                        |  |
| 098.32                      | Gonococcal prostatitis (chronic)                      |  |
| 131.03                      | Trichomonal prostatitis                               |  |

| ICD-10 codes for Prostatitis |   |
|------------------------------|---|
| N41.0                        | Acute prostatitis                             |
| N41.1                        | Chronic prostatitis                           |
| N41.3                        | Prostatocystitis                              |
| N41.4                        | Granulomatous prostatitis                     |
| N41.8                        | Other inflammatory diseases of prostate       |
| N41.9                        | Inflammatory disease of prostate, unspecified |
| A54.22                       | Gonococcal prostatitis (acute or chronic)     |
| A59.02                       | Trichomonal prostatitis                       |

# **IV. Suggested Readings**

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# WAIVER GUIDE

Updated: Sep 2015

Supersedes Waiver Guide of Nov 2011

By: Lt Col An Duong (RAM 16) and Dr. Dan Van Syoc

Reviewed by Lt Col Eric Barnes, AF/SG consultant for Nephrology

# **CONDITION:**

Proteinuria & IgA Nephropathy (Sep 2015)

# I. Waiver Considerations.

Benign forms of proteinuria are routinely waived for all flying classes if it is deemed to be benign after specialty consultation. IgA nephropathy is disqualifying for FC I/IA, II, III, and SWA duties if the proteinuria exceeds 200 mg/24 hours. Chronic nephritis with renal function impairment and nephrosis worse than mild are disqualifying for all flying and special operational duties and require an MEB prior to waiver submission. Certain ACE inhibitors and ARBs are approved for aircrew use, as are a number of statins, though the role of the latter in IgA nephropathy is unclear. Corticosteroid therapy is not waiverable. If significant hematuria is also present, please consult with the waiver guide for hematuria for assistance.

Table 1: Waiver potential for proteinuria and IgA Nephropathy

| Flying Class (FC)    | Condition  | Waiver Potential           |
|----------------------|--|----------------------------|
|                      |  | Waiver Authority           |
| I/IA                 | Proteinuria without evidence of                            | Yes                        |
| Untrained II/III/SWA | renal disease or hypertension                              | AETC                       |
|                      | Proteinuria without evidence of                            |                            |
|                      | renal disease, but with hypertension*+∫                    | AETC                       |
|                      | Proteinuria with evidence of renal disease with or without | No                         |
|                      | hypertension   | AETC                       |
|                      | IGA Nephropathy with proteinuria                           |                            |
| II/III               | Proteinuria without evidence of                            | Yes                        |
| SWA                  | renal disease or hypertension                              | MAJCOM                     |
|                      | Proteinuria without evidence of                            |                            |
|                      | renal disease, but with hypertension *+#                   | MAJCOM                     |
|                      | Proteinuria with evidence of                               |                            |
|                      | renal disease with or without hypertension *+#             | Yes<br>MAJCOM              |
|                      | IGA Nephropathy with proteinuria +                         |                            |
| ATC/GBO              | Chronic nephritis with renal                               | Maybe, after MEB<br>MAJCOM |
|                      | function impairment  | IVIAJCOM                   |
|                      | Nephrosis worse than mild                                  | Maybe, after MEB<br>MAJCOM |

<sup>\*</sup> Hypertension controlled on low dose HCTZ, chlorothiazide, triamterene, lisinopril, ramipril, benazepril, telmisartan or losartan may be considered for waiver.

AIMWTS review in Sep 2015 for the diagnoses of proteinuria and IgA nephropathy revealed a total of 95 cases, with 19 of those resulting in a disqualification disposition. Breakdown of the cases revealed: 14 FC I/IA cases (6 disqualified), 43 FC II cases (5 disqualified), 28 FC III cases (6 disqualified), 7 ATC/GBC cases (1 disqualified), and 3 MOD cases (1 disqualified).

<sup>+</sup> No indefinite waivers.

<sup>#</sup> FC IIA waiver can also be considered with HCTZ combined with lisinopril, ramipril, benazepril, telmisartan or losartan; atendol alone or in combination; nifedipine (coat-core or GITS) alone or in combination; or amlodipine alone or in combination.

J Waiver for FC I/IA and untrained FC II and FC III may be considered if sustained HTN control well documented, on low standard dosage, no evidence of end organ damage and no side effects.

# II. Information for Waiver Submission.

The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for <u>initial waiver</u> for proteinuria and/or IgA nephropathy should include the following:

- A. Complete history of the problem to include all consultants seen.
- B. Physical exam results.
- C. Labs all urinalysis tests to include microscopic results, BUN/Cr, 24 hour urine, renal biopsy results if done.
- D. Nephrologist consultation report if completed.
- E. Current treatment to include all medications and dates started.
- F. Results of MEB if aviator has IgA nephropathy, or nephropathies, or nephritis.
- G. Detail of all other medical problems, if applicable.

The aeromedical summary for <u>waiver renewal</u> for proteinuria and/or IgA nephropathy should include the following:

- A. Updated history since last waiver
- B. Physical exam results.
- C. Labs all urinalysis tests, other labs and additional renal biopsies since last waiver.
- D. Nephrologist consult report if new one accomplished.
- E. Current treatment to include all medications and dates started.

## III. Overview.

Proteinuria is an early and sensitive marker for renal damage in many types of chronic kidney disease. It characterizes most forms of glomerular injury, but is not necessarily diagnostic for renal injury. Urinalysis is a common test in the clinic and is performed for many reasons. Urinalysis is often part of a screening exam such as school physicals, preplacement exams and flight physicals. Annual screening for proteinuria is no longer felt to be cost-effective in the general population for those less than 60 years of age, but the National Kidney Foundation recommends regular surveillance for those at risk of kidney disease. Risk factors for kidney disease include family history of kidney disease, diabetes, hypertension, ethnic minority, obesity, and metabolic syndrome.<sup>2, 3</sup> For patients at risk, it is important to detect disease early in its course as current therapy can significantly slow progression of proteinuric chronic kidney disease.

Urinary protein excretion in the normal adult should be less than 150 mg/day. If the excretion exceeds this level beyond a single measurement, the patient needs to be evaluated for possible glomerular disease. Transient proteinuria can occur in up to 7% of women and 4% of men and is often associated with fever or exercise. Such benign proteinuria nearly always resolves on follow-up; thus, isolated proteinuria is normally not evaluated unless confirmed on repeat analysis. The gold standard for quantification of proteinuria is a 24 hour urine collection. It is important to note that 24 hour collections are inconvenient for most patients and can be inaccurate due to over or under collecting of urine. For patients with albuminuria on urinalysis, a urine albumin/creatinine

(UACR) (normal  $\leq$  30 mg/L) or urine protein/creatinine (UPCR) (normal  $\leq$ 0.150) should be obtained for further evaluation.<sup>2</sup>

Common causes of proteinuria in an adult population include isolated proteinuria, orthostatic proteinuria, conditions causing nephritis, and as a result of systemic illness. Isolated proteinuria can result from problems such as febrile illness, other physiologic stress or vigorous exercise or from abnormal production in conditions including myeloma and monoclonal gammopathies, or from toxins such as cadmium.

Orthostatic proteinuria is not an uncommon condition in adolescents and young adults but it is rare after age 30. This condition is characterized by an increase in protein excretion in the upright position, but a normal excretion (< 50 mg/8 hours) when supine. This postural response contrasts with most patients with glomerular disease who will normally demonstrate a modest reduction in protein excretion while supine, but commonly not to normal levels. Glomerular disease may initially present with mild manifestations therefore people with orthostatic proteinuria should have a follow-up evaluation after one year to evaluate for persistence or progression.<sup>4</sup>

Patients with signs or symptoms suggestive of glomerular disease, such as persistent proteinuria or hematuria and/or impaired renal function, should be considered for a renal biopsy in order to obtain a diagnosis. The risks associated with a biopsy, such as bleeding, are minimal with experienced clinicians. The most frequent adult primary glomerular disorders are IgA nephropathy followed by focal and segmental glomerulosclerosis (FSGS) and then membranous nephropathy.<sup>5</sup>

IgA nephropathy was first described by Berger and Hinglais in 1968. It is now the most prevalent primary chronic glomerular disease worldwide and is defined as an immune-complex-mediated disease characterized by the presence of glomerular IgA deposits accompanied by a variety of histopathologic lesions.<sup>6</sup>

IgA nephropathy presents with episodic hematuria and often follows an upper respiratory infection – so called "synpharyngitic hematuria". It has macroscopic and microscopic forms; the latter is the more common form seen in adults. Between episodes of macroscopic hematuria, the urinalysis is often normal. The presence or absence of increasing proteinuria at the time of clinical diagnosis often determines whether patients with asymptomatic hematuria are biopsied.<sup>7,8</sup> The disease was initially considered a benign form of hematuria, but it is now clear that up to 50% of patients may progress to end-stage renal disease.<sup>6,9</sup> The remaining patients may enter a sustained clinical remission or have persistent low grade hematuria or proteinuria. The prognosis is variable and the outcome difficult to predict with accuracy in individual patients. It can present at any age, but is more common in the second and third decades. There is a male to female ratio ranging from 2:1 to 6:1 in Europe and the US. Ethnically, Caucasians and Asians are much more prone to this disease than are African Americans.<sup>6</sup>

IgA nephropathy may present in one of three ways. About 40-50 percent of patients present with one or more episodes of gross hematuria usually following an upper respiratory infection. Another 30-40 percent have microscopic hematuria and mild proteinuria incidentally detected on a routine examination. Less than 10 percent of patients present with nephrotic syndrome, or with acute rapidly progressive glomerulonephritis characterized by hematuria, edema, hypertension and renal insufficiency. A definitive diagnosis can only be made by renal biopsy and immunohistologic

examination. In patients who have isolated hematuria, a renal biopsy is usually performed only if there are signs suggestive of severe disease or progressive protein excretion above 0.5 to 1 gram/day, an elevated plasma creatinine, or hypertension. A skin biopsy looking for IgA deposition in the dermal capillaries has not proven to be predictive in IgA nephropathy. <sup>10</sup>

While there is no recognized cure for this disease, there are treatment options that slow disease progression, and up to 23% of patients will show a complete remission. A very important part of the evaluation of patients with IgA nephropathy is to predict their risk for progression to renal failure. Risk factors for progressive renal failure include: elevated serum creatinine above 2.5 mg/dL at the time of diagnosis, hypertension, and persistent proteinuria above 0.5 to 1 g/day. The relationship between increasing proteinuria and a worse prognosis is probably a reflection of proteinuria as a marker for the severity of glomerular disease. The rate of progression is low among patients excreting less than 500 mg/day and fastest among those excreting more than 3.0 to 3.5 g/day of protein.

There are two separate approaches to the treatment of IgA nephropathy. General interventions to slow progression of renal disease that are not specific to IgA nephropathy include blood pressure control, angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) in patients with proteinuria. Reduction in proteinuria is the hallmark of effective treatment in preserving renal function in other types of nondiabetic proteinuric renal diseases. <sup>6, 12</sup> Corticosteroids can be used in advanced cases of IgA nephropathy. Statin therapy for lipid-lowering is recommended in the majority of chronic kidney disease patients to lower cardiovascular risk and possibly reduce disease progression. Fish oil has been studied but its role in treating IgA nephropathy is not well defined. <sup>9</sup> Some studies indicate that it may be useful for reducing renal inflammation and glomerulosclerosis.

The treatment of choice for individuals who progress to end-stage renal disease is preemptive renal transplantation – that is, transplantation before they require hemodialysis. Many of these patients are younger and otherwise healthy. Transplantation provides a reasonable quality of life and a lifespan longer than that of the hemodialysis patient. Kidney disease recurrence does occur in transplanted kidneys, however transplant centers are accustomed to monitoring patients at risk. Nearly one-third of transplant recipients will develop a clinically apparent recurrence of the disease in the transplanted kidney. The rate of recurrence is equal between cadaveric and living donors.

## IV. Aeromedical Concerns

Regarding proteinuria, flyers will be disqualified when diagnosed with "Proteinuria under normal activity (at least 48 hours post strenuous exercise) greater than 200 mg in 24 hours, or protein to creatinine ratio greater than 0.2 (by random urine sample), or other findings indicative of urinary tract disease unless consultation determines the condition to be benign. "In other words, if the protein loss can be explained by a relatively benign process or is stable (protein cannot be > 500mg/24 hours), the aeromedical concerns would be negligible and waiver is favorably considered. For IgA nephropathy, the aeromedical concerns would be related to the renal function, any symptoms, and the medications being used. For most flyers, a return to flying (waiver) would be in order once the disease is in remission and requires no medication. In those with a more chronic or indolent form, the disease is usually one that is slowly progressive. Typically such

patients are treated with ACE inhibitors to preserve renal function, and a waiver will likely be granted if the patient is otherwise stable.<sup>14</sup>

| ICD-9 Codes for Proteinuria |                            |
|-----------------------------|----------------------------|
| 791.0                       | Proteinuria                |
| 583.81                      | Nephropathy, not specified |
| 583.9                       | IgA nephropathy            |

| ICD-10 Codes for Proteinuria |   |  |
|------------------------------|---|--|
| R80.9                        | Proteinuria, unspecified                              |  |
| N08                          | Glomerular disorders in diseases classified elsewhere |  |
| N02.8                        | IgA nephropathy                                       |  |

### V. References.

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## WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of Jul 2014

By: Lt Col Lance Nussbaum (RAM 19) and Dr Dan Van Syoc

Reviewed by Lt Col Jeffrey Bidinger, AF/SG consultant for dermatology, and AFMSA staff

#### **CONDITION:**

Psoriasis & Psoriatic Arthritis (Jan 2018)

# I. Waiver Consideration.

For entry into the US Air Force, a current or past history of psoriasis is disqualifying (DoDI 6130.03); this would definitely impact those individuals applying for initial flying training as well. The diagnosis of psoriasis is disqualifying for flying class I/IA, II, III, and SWA duties (MSD P28). For ATC and GBO personnel, psoriasis is only disqualifying if not controlled by treatment, or controllable only with systemic medications or UV light therapy (MSD P26). Use of personal protective equipment is also going to be a big factor for all career fields for members with psoriasis. Psoriatic arthritis is not mentioned by name as disqualifying for aviation service, but "arthritis of any type of more than minimal degree, which interferes with the ability to follow a physically active lifestyle, or may reasonably be expected to preclude the satisfactory performance of duties" is disqualifying for all flying classes as well as for ATC, GBO, and SWA duties. Also, a medical evaluation board (MEB) is required if the psoriasis is extensive and not controlled or controllable only with potent cytotoxic/systemic agents (methotrexate, cyclosporine, oral retinoids, PUVA and immune modulating drugs, to include TNF-alpha inhibitors).

**Table 1: Waiver Potential for psoriasis and psoriatic arthritis** 

| Flying     | Condition/Treatment for                                       | Treatment for                 | Waiver Potential  |
|------------|---|-------------------------------|-------------------|
| Class (FC) | Psoriasis   | Psoriatic Arthritis           | Waiver            |
| (1 C)      |   |                               | Authority         |
| I/IA       | History of psoriasis at any time                              | History of psoriatic          | No                |
|            | whether or not under current                                  | arthritis currently           | AETC              |
|            | therapy of any kind   | treated or not                |                   |
| II/        | Topical steroids, calcipotriene,                              | NSAIDS,                       | Yes               |
| III/SWA*   | topical retinoids   | sulfasalazine                 | MAJCOM            |
|            | (tazarotene),UVB  |                               |                   |
|            |   |                               | Yes <sup>\$</sup> |
|            | Etanercept, adalimumab,                                       | Etanercept,                   | AFMRA             |
|            | infliximab, or tacrolimus                                     | adalimumab, or                |                   |
|            | (topical)   | infliximab, or                |                   |
|            |   | tacrolimus (topical)          |                   |
|            |   | 0 1 4 11                      | No                |
|            | Discounting and adducted                                      | Oral retinoids,               | AFMRA             |
|            | Pimecrolimus, oral retinoids,                                 | methotrexate,                 |                   |
|            | methotrexate, cyclosporine, and other immunomodulators        | cyclosporine, and other       |                   |
|            | (except TNF-alpha inhibitors                                  | immunomodulators              |                   |
|            | above), PUVA  | (except TNF-alpha             |                   |
|            | 100vc), 1 0 v / 1   | inhibitors above)             |                   |
| ATC/GBO    | Topical steroids, calcipotriene,                              | NSAIDS,                       | Yes               |
|            | topical retinoids (e.g.                                       | sulfasalazine                 | MAJCOM            |
|            | tazarotene), UVB  |                               |                   |
|            |   |                               |                   |
|            | Etanercept, adalimumab,                                       |                               | Yes <sup>\$</sup> |
|            | infliximab or tacrolimus                                      | Etanercept,                   | AFMRA             |
|            | (topical)   | adalimumab,                   |                   |
|            |   | infliximab, or                |                   |
|            |   | tacrolimus (topical)          |                   |
|            | Dimogralimus and national de                                  | Onel mating ide               | No                |
|            | Pimecrolimus, oral retinoids, methotrexate, cyclosporine, and | Oral retinoids, methotrexate, | No<br>AFMRA       |
|            | other immunomodulators (except                                | cyclosporine, and             | AUMINA            |
|            | TNF-alpha inhibitors above),                                  | other                         |                   |
|            | PUVA  | immunomodulators              |                   |
|            |   | (except TNF-alpha             |                   |
|            |   | inhibitors above)             |                   |

<sup>\*</sup> All initial training applicants to be treated as FC I/IA

AIMWTS review in Jan 2018 revealed a total of 382 cases with a psoriasis or psoriatic arthritis diagnosis. Of those, 61 were disqualified; however, only 39 of the disqualifications were related to

<sup>\$</sup> If on TNF-alpha inhibitor, waiver will be restricted (not worldwide qualified, TDY requires access to transport and refrigeration of etanercept/adalimumab). MEB is required. Observe for 3 to 6 months on therapy before consideration of waiver to allow for assessment of response, possible adverse effects. Forward to ACS for review.

psoriasis or psoriatic arthritis disorders. The other 22 disqualifications were primarily due to other diagnoses besides psoriasis/psoriatic arthritis. There were 9 FC I/IA cases (6 disqualified), 167 FC II cases (5 disqualified), 5 RPA pilot cases (1 disqualified), 186 FC III cases (46 disqualified), 12 ATC/GBC cases (1 disqualified), and 3 MOD cases (2 disqualified).

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

# The AMS for <u>initial and renewal waivers</u> must include:

- A. History to include extent of lesions, locations, symptoms, and a description of current therapy, all medications including dosage, and frequency, and comments addressing interference with use of aviation equipment or jeopardy to safe mission accomplishment. If arthritis, then in addition to joints involved should address any interference with flight controls and egress ability.
- B. Physical joints involved, surface area affected and description of lesions, body surface area involved (palm of hand = 1% BSA and can be used to estimate).
- C. Copy of dermatology consultation.
- D. All cases of psoriatic arthritis should be evaluated by a rheumatologist. These cases need to have results of radiographs for hands, feet, and any symptomatic joints.
- E. Laboratory testing for initial waiver for psoriatic arthritis: complete blood count, sedimentation rate, C-reactive protein.
- F. If topical vitamin  $D_3$  (calcipotriene) is used, verify with the aviator the amount of topical vitamin  $D_3$  cream use is less than 100 gm a week. Also baseline normal renal function should be confirmed prior to usage.
- G. If on etanercept/adalimumab/infliximab, for initial waiver, results of IPPD or Quantiferon releasing assay required.
- H. If on etanercept/adalimumab/infliximab, then MEB required.

## III. Overview.

Psoriasis: Psoriasis affects about two percent of the population in the United States, with approximately 150,000 new cases diagnosed per year, and is equally common in males and females. Approximately 80% of all psoriasis patients have mild to moderate disease with the remainder having moderate to severe disease.<sup>1</sup> Onset is a lifelong threat as it has been documented at birth and up to age 108, with peak incidence at 22.5 years. An early onset (before age 15) predicts more severe disease relative to the percentage of body surface involved and response to therapy.<sup>2</sup> While looked at as a simple dermatological disease, recent research has demonstrated a far more complex immune-mediated disease process. Psoriasis is associated with arthritis and inflammatory bowel disease. It is also an independent risk factor for diabetes, hypertension, coronary artery calcification, myocardial infarction, lymphoma, and depression.<sup>3-5</sup> An important issue to consider is that the impact of psoriasis on quality of life of affected individuals is comparable to other disorders such as cancer, diabetes, heart disease, and depression.<sup>6</sup>

Psoriasis is a hyperproliferation and immune regulation disorder. Hyperproliferation is seen with increased numbers of epidermal cells, increased number of cells undergoing DNA synthesis, and an

increased turnover of epidermal cells.<sup>8</sup> A T-cell immune response is noted with increased T-cells seen in the skin.<sup>9</sup> TNF-alpha, gamma interferon, and various interleukins are overexpressed in psoriasis patients.<sup>10</sup> Dendritic cells play a key role in this immune response as they are activated by environmental factors and subsequently produce interferon alpha and stimulate T-cell differentiation in the dermal layers.<sup>11, 12</sup> Current psoriasis therapies attempt to address this complex interaction.

Morphologic appearance and distribution are keys to diagnosis, as well as the Auspitz phenomenon (after mechanical removal of a scale, small droplets of blood appear on the erythematous surface). Typical plaques are bilateral and symmetric, erythematous, dry, and scaling (silvery white scale) that favor extendor surfaces. Presentation may vary from a few localized psoriatic plaques to generalized skin involvement, to a life-threatening pustular psoriasis. The course of psoriasis is chronic and unpredictable. Plaques are the most common form of the disease and most (65%) have mild disease. While genetics appear to play a variable role in the development of psoriasis, the most significant triggers include environmental and behavioral factors such as cold weather, physical trauma, infections, stress, and drugs (lithium, beta-adrenergic blockers, antimalarial agents, angiotensin-converting enzyme inhibitors, and corticosteroid withdrawal).<sup>2, 7, 8, 9, 13</sup> Given the increased deployment tempo to Africa, antimalarials are being prescribed to more and more military members. The 4-aminiquinolone compounds (chloroquine and hydroxychloroquine) are known to exacerbate existing psoriasis/psoriatic arthritis. In one review, 20 of 48 (42%) soldiers given cholorquine experienced an exacerbation of their psoriasis. Psoriasis is considered a contraindication for the use of chloroquine and hydroxychloroquine.<sup>14</sup>

Psoriasis distribution is usually symmetrical, and favors the elbows, knees, scalp, and sacrum. Palms, soles, nails and intertriginous (inverse psoriasis) areas can be involved. Guttate psoriasis is a form of psoriasis with typical lesions the size of water drops, 2 to 5 mm in diameter, that occur as an abrupt eruption following an acute infection, such as streptococcal pharyngitis, and usually in patients under 30. Chief complaints of psoriasis include: disfigurement, lowered self-esteem, being socially ostracized, pruritus and pain (especially palms, soles, and intertriginous areas), excessive scale, heat loss (with generalized lesions), and arthralgias.

Dermatologists may grade the severity of psoriasis on body surface area (BSA); less than three percent is mild, three to 10 moderate, and greater than 10 percent severe.<sup>15</sup> The palm of the hand equals one percent of the skin. However, the severity of psoriasis is also measured by how psoriasis affects a person's quality of life. Psoriasis can have a serious impact even if it involves a small area, such as the palms of the hands or soles of the feet.

Treatment includes topical steroids, topical tar, topical vitamin D<sub>3</sub> (calcipotriene [Dovonex®]), topical retinoid (tazarotene [Tazorac®]), topical calcineurin inhibitors (pimecrolimus and tacrolimus), phototherapy, and systemic agents such as methotrexate, acitretin, or newer biologic immune response modifiers, such as adalimumab, etanercept and infliximab, for moderate to severe disease. Newer immunosuppressive agents such as ustekinumab (Stelara®), secukinumab (Cosentyx) or ixekizumab (Taltz) may also be considered, but are not approved for use in aircrew. Goal of therapy is to decrease body surface area, decrease erythema, scaling and thickness of plaques, improve quality of life and avoid adverse effects. 17

Approximately 70 to 80% of all patients with psoriasis can be treated adequately with use of topical therapy. In cases of moderate-to-severe psoriasis (e.g. affecting large surface areas), the use of phototherapy, systemic drugs or both are more likely to be required. Management of each case needs to be individualized and may involve combinations of modalities.<sup>5</sup>

<u>Psoriatic Arthritis</u>: Psoriatic arthritis is one of the seronegative spondyloarthritis disorders, and as such, it is associated with a negative rheumatoid factor. It may precede (in children only), accompany, or more often, follow skin psoriasis. Estimates of the prevalence of psoriatic arthritis among individuals with psoriasis vary from 4 to 6 percent up to 30 percent; equal in female and male. Nail involvement occurs in more than 80% of patients with psoriatic arthritis, compared with 30% of patients with uncomplicated psoriasis. Approximately 20% of individuals with psoriatic arthritis develop destructive and potentially disabling disease. 19

As in psoriasis, proinflammatory cytokines and activated T-cells are found in the affected tissues; namely synovium and joints. Joint symptoms include stiffness, inflammation and swelling. The most common areas involved include the distal interphalangeal joints and the spine. Pain is usually improved with physical activity. Over half of patients with psoriatic arthritis have radiographic abnormalities and nearly half of those recently diagnosed will have erosions within two years. There are five recognized presentations of psoriatic arthritis: 13

**Table 2: Presentation of Psoriatic Arthritis** 

| Туре                                  | Percentage of all psoriatic arthritis | Features                     |
|---------------------------------------|---------------------------------------|------------------------------|
| Asymmetric oligo-arthritis            | 60 - 70                               | Joints of fingers and toes   |
| (involving DIPs, PIPs and MCPs)       |                                       | ("sausage finger")           |
| Symmetric polyarthritis               | 15                                    | Clinically resembles         |
|                                       |                                       | rheumatoid arthritis,        |
|                                       |                                       | rheumatoid factor negative   |
| Distal interphalangeal joint disease  | 5                                     | Mild, chronic, associated    |
| only                                  |                                       | with nail disease            |
| Destructive poly arthritis (arthritis | 5                                     | Osteolysis of small bones of |
| mutilans)                             |                                       | hands and feet; gross        |
|                                       |                                       | deformity; joint subluxation |
| Ankylosing spondylitis                | 5                                     | With or without peripheral   |
|                                       |                                       | joint disease                |

Treatment usually begins with nonsteroidal anti-inflammatory drugs (NSAIDs). Sulfasalazine, etanercept (Enbrel®), adalimumab (Humira®) and infliximab (Remicade®) are other waiverable medications used to treat psoriatic arthritis. Etanercept in one study resulted in 20% and 50% improvement in 59% and 37% of individuals, respectively. Although etanercept may be administered at a dose of 25 mg twice a week, a dosage schedule of 50 mg once a week has shown similar efficacy and simplifies the regimen, particularly with the autoinjector dosage form. The drug is given in rotating fashion over the subcutaneous tissue of the thighs. Etanercept must be kept refrigerated between 36° to 46°F, for it degrades rapidly even at room temperature. Adalimumab also has demonstrated efficacy in the treatment of psoriatic arthritis and is FDA-approved for this indication. Typical dosing is 40 mg injected subcutaneously every other week. Handling of the

drug is similar to etanercept, but refrigeration requirements have recently changed (see www.humira.com).<sup>23</sup> Additional medications used for treatment such as methotrexate and cyclosporine are not waiverable.<sup>17, 21</sup>

#### IV. Aeromedical Concerns.

The main concerns are interference with wear of protective aviation equipment; distraction by pruritus or pain; triggering or exacerbation of the disease through repeated occupational trauma to the skin (Köebner's phenomenon); use of treatment medications that are incompatible with flying duties; unavailability of treatment in a deployed setting (ultraviolet light therapy); frequency of follow-up requiring excessive time lost from flying duties; and psychological factors. Although psoriasis usually spares the face and may not affect wear of a mask, scalp involvement is possible and may interfere with helmet use. Involvement of palms and soles may interfere with use of flight controls. Discomfort from pruritus or pain can be significant and the resulting distraction may jeopardize flight safety. These symptomas may also interfere with proper crew rest and lead to a subtle degradation of performance. Köebner's phenomenon may be caused by repeated rubbing or pressure including wear of a helmet or prolonged sitting in the cockpit.

While most topical treatments are well tolerated with few side effects, some may cause an irritant skin reaction. UVB phototherapy is well tolerated except for risk of burning and skin dryness. PUVA (oral photochemotherapy) short term side effects include nausea, dizziness, headache, pruritus, cutaneous and eye photosensitivity and long term side effect of increased risk of skin cancer. Joint involvement may interfere with use of flight controls, be a distraction due to discomfort, and limit egress ability. Some forms of therapy (e.g. ultraviolet light) may require several treatments per week, are not typically available in a deployed setting, and may require excessive time lost from flying duties. It is important to maintain awareness of the psychological aspect of this potentially disfiguring disease and its effect on the aviator's social situation.

Systemic treatments may have a range of significant side effects that are incompatible with flying duties in addition to the disqualifying nature of the severe forms of psoriasis. Methotrexate, because of serious toxicity involving multiple organs (e.g., lung, central nervous system), is not waiverable. Of the toxicities associated with anti-TNF therapy, those related to immunosuppression have been of greatest concern. The increased risk of developing demyelinating disease appears to be well within aeromedical standards. The same is true of lymphoma, and the latter would be unlikely to be of particular aeromedical concern. There is inconclusive evidence of possible increased risk for congestive heart failure in anticytokine therapy. Individuals on anti-TNF therapy are at greater risk of infectious complications, to include bacterial and granulomatous infections. Anti-TNF therapy should never be initiated in the setting of an infection, and before anti-TNF therapy is begun, a baseline HIV, hepatitis B and C profile and quantiferon gold TB test is required; for a positive quantiferon TB, antituberculous prophylaxis should be initiated. <sup>21, 23</sup> Recommendations regarding duration of INH prophylaxis before beginning TNF-alpha inhibitors have been inconsistent. At the very least, consider withholding TNF-alpha inhibitors until an appropriate preventive regimen is established. <sup>24</sup>

| ICD-9 Codes for Psoriasis and Psoriatic arthritis |                       |  |
|---|-----------------------|--|
| 696.0   | Psoriatic arthropathy |  |
| 696.1   | Psoriasis             |  |

| ICD-10 Codes for Psoriasis and Psoriatic arthritis |                             |  |
|--|-----------------------------|--|
| L40.59   | Other psoriatic arthropathy |  |
| L40.8  | Other psoriasis             |  |

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# **WAIVER GUIDE**

Updated: Jul 2014

Supersedes Waiver Guide of Apr 2010

By: Lt Col Niraj Govil (RAM XV) and Dr Dan Van Syoc

Reviewed by Col Kent McDonald, psychiatrist and chief of the ACS Neuropsychiatry Branch

### **CONDITION:**

Psychotic Disorders (Jul 2014)

#### I. Waiver Consideration.

Psychotic disorders, as well as delirium and other cognitive disorders are disqualifying for all flying classes to include ATC/GBO and SWA duties. Waiver may be considered after the patient has been free of psychotic symptoms and off all mental health treatment including psychotropic medications for one year. A psychotic episode caused by alcohol, and occurring during the course of alcohol abuse or alcohol dependence, is considered for waiver in accordance with the waiver requirements for an alcohol use disorder (DSM V). A psychotic episode caused by alcohol, but not in the setting of alcohol abuse or dependence, is considered for waiver according to the guidance in this waiver guide. When the inducing substance is illicit, a return to flying is unlikely. In all other cases of substance-induced psychotic disorders, there must be clear evidence (history, physical examination, and laboratory evaluation) that the substance (e.g. prescribed medication producing an idiosyncratic reaction or an unintentional overuse of an over-the-counter medication) caused the psychosis. In cases of a psychotic disorder due to a general medical condition waiver, may be considered once the psychosis and the medical condition have completely resolved and are unlikely to recur, if the medical condition itself is waiverable.

Schizophrenia, schizoaffective disorder, delusional disorder, brief psychotic disorder without marked stressor(s), and shared psychotic disorder are permanently disqualifying for flying and special operational duties. Antipsychotic medications and close psychiatric monitoring are incompatible with flying duties. An MEB is required for any psychotic episode that is not due to a clearly identifiable and avoidable cause. Any psychotic episode other than those with a brief duration, good prognosis and clearly identifiable and reversible cause must meet MEB.

Before submitting the case for waiver consideration, the base-level flight surgeon must first discern whether the condition is unsuiting vs. unfitting for service. If the Airman requires a fit/unfit determination, the case needs MEB action; if the Airman requires suited/unsuited determination, the case then needs consideration of an administrative separation or discharge via the chain of command.

**Table 1: Waiver potential for psychotic disorders** 

| Flying Class (FC) | Waiver Potential <sup>1</sup> | ACS Evaluation/Review     |
|-------------------|-------------------------------|---------------------------|
|                   | Waiver Authority              |                           |
| I/IA              | No                            | Only if requested by AETC |
|                   | AETC                          |                           |
| II/III            | Yes <sup>2</sup>              | Yes                       |
|                   | MAJCOM                        |                           |
| ATC/GBO/SWA       | Yes <sup>2</sup>              | Yes                       |
|                   | MAJCOM                        |                           |

<sup>1</sup> No indefinite waivers.

AIMWITS search in Jul 2014 revealed a total of 19 members with a submitted aeromedical summary containing a diagnosis of psychosis. Breakdown of the cases revealed: 1 FC I/IA cases (disqualified), 10 FC II cases (8 disqualified), 6 FC III cases (3 disqualified), and 1 ATC/GBC case (disqualified).

# II. Information Required for Waiver Submission.

**Submitting a Mental Health Waiver Guide:** 

# Step 1 - Is the aviator ready for waiver submission?

| A. | Waiver is submitted when 1) the member is asymptomatic and 2)                                      |
|----|--|
|    | medications/psychotherapy treatment have been completed, as applicable to diagnostic               |
|    | category, for the specified time-frame below (Note: psychotherapy "booster sessions", and          |
|    | sometimes SSRIs, are permissible and often advisable after initial symptom resolution):            |
|    | 1 Year—Psychotic Disorders & Somatoform Disorders  |
|    | 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior                                     |
|    | Discretion of Flight Surgeon—Adjustment Disorders & V-Codes requiring waiver                       |
|    | For Traumatic Brain Injury cases, please refer to TBI Waiver Guide                                 |
|    | For aviators with any other psychiatric disorders, please refer to AFI 48-123 and ACS Waiver Guide |
| B. | To be considered for an aeromedical waiver, any disqualifying condition must meet the              |
|    | following criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg.31):                    |
|    |  |
|    | Not pose a risk of sudden incapacitation   |
|    | Pose minimal potential for subtle performance decrement, particularly with regard to the           |
|    | higher senses  |
|    | Be resolved, or be stable, and be expected to remain so under the stresses of the aviation         |
|    | environment  |
|    | If the possibility of progression or recurrence exists, the first symptoms or signs must be        |
|    | easily detectable and not pose a risk to the individual or the safety of others                    |
|    | Cannot require exotic tests, regular invasive procedures, or frequent absences to monitor          |
| _  | for stability or progression   |
|    | Must be compatible with the performance of sustained flying operations                             |

<sup>2</sup> For all UNTRAINED individuals (FC I/IA, FC II/III, and ATC/GBO/SWA), a waiver is NOT considered.

# Step 2 - Before beginning the Aeromedical Summary (AMS), Flight Surgeon must obtain Mental Health consultation and ensure it contains items specified below: **Instructions for the Mental Health Provider** The mental health evaluation must include a **comprehensive written report** addressing: Consultation must address each criteria in Step 1B Clinical mental health history (description of symptoms, treatment modality, frequency and compliance with treatment, relevant personal and family history, and perceived impact on occupational duties) Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination) Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile...) \*\* for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results\*\* Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental illness) Current and past aviation related duties and any history of current and past occupational performance difficulties (to include perceived impact of mental health condition on performance of duties) Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep) Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended neuropsychological tests. Current mental status Diagnosis Motivation to fly or engage in special duty operations (past and current) Recommendation for future psychological and medical treatment Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties) Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand for shipment to ACS Neuropsychiatry Branch **Step 3 - Items for the Flight Surgeon to include in the AMS:** AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safety Summarize Mental Health history and focus on occupational impact \*\* If 2 or more months have passed since the comprehensive evaluation/report was completed, the flight surgeon should address how the member has done since and consult with the mental health provider if the member has been seen at mental health since the evaluation\*\*

compliance, response, clinical course since termination)

Medication history (dates of initial prescription and termination, reason for termination, dosage,

Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile...)

\*\* for alcohol cases, please comment on Carbohydrate-deficient transferrin (CDT) results\*\*

| Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if  |
|---|
| possible - please address current state of any triggers for the mental illness) Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep) |
| Current mental status   |
| Diagnosis   |
| Motivation to fly (past and current)  |
| Recommendation for future psychological and medical treatment   |
| Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
| Items to complete the waiver package: Letter of support from command  |
| Comprehensive mental health written-report  |
| Confirm mental health has made copies of chart(s) and testing. When requested send to:  |
| ACS Aerospace Medicine Branch, USAFSAM/FECA<br>c/o Neuropsychiatry Branch<br>2510 Fifth Street Bldg 840<br>Wright Patterson AFB, OH 45433-7913<br>Fax: (937) 904-6296 DSN: 674-9296 |
|   |

Please feel free to contact the ACS Neuropsychiatry Branch with questions: TSgt Tonya Merriweather: DSN 798-2703, SSgt Krista Traut 798-2738, or Mr. John Heaton: 798-

2766

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for initial waiver for psychotic disorders should include the following:

- A. History An aeromedical summary detailing history of the disorder and all treatments administered, the current status of any social, occupational, administrative or legal problems associated with the case, and an analysis of the aeromedical implications of this particular case history.
- B. Treatment medications and therapy used for the psychotic disorder and any other psychiatric conditions. Are there any side effects due to the medication? A good laboratory examination to include a toxicology screen and blood alcohol level are vital to the waiver. Psychosis almost always results in an emergency room visit so ensure the records are attached.
- C. Psychiatry/psychology consultation: Need all treatment notes from treating mental health professional as well as an MEB-type narrative summary of the mental health record.
- D. Report of all psychological testing, if performed.
- E. Letter of support from squadron commander.

The AMS for waiver renewal for psychotic disorders should include the following:

- A. History interim history since last waiver.
- B. Treatment current therapy for the condition, if any.

C. Psychiatry/psychology consultation report(s) if accomplished since last waiver request.

#### III. Overview.

Schizophrenia Spectrum and Other Psychotic Disorders are defined by one or more of the following: delusions, hallucinations, disorganized thinking (will be evident through speech), grossly disorganized behavior or abnormal motor movement (catatonia) and negative symptoms. 1.

Psychotic states are periods of high risk for agitation, aggression, impulsivity, and other forms of behavioral dysfunction. 2 They can occur as standalone psychiatric disorders or psychosis can be seen in conjunction with other psychiatric and medical disorders. Schizophrenia is probably the best-known psychotic disorder, but is extremely rare in aviators. Other recognized psychotic disorders include schizophreniform disorder, schizoaffective disorder, delusional disorders, and brief psychotic disorder. It is difficult to assess the prevalence of psychotic disorders in the population as these people often do not seek medical care. Some recent estimates of the lifetime prevalence of such disorders are as high as 3.0% of the US population. 3

Due to the multiple screening processes involved in aircrew selection; it is unlikely that someone with a psychotic disorder would ever be selected for training. It is recognized that most serious psychotic conditions begin in adolescence with initial subtle symptoms that may be very hard to detect. This early period often consists of nonspecific symptoms in otherwise normal functioning people and detection can be very difficult.<sup>4</sup> As with all mental health conditions, there are various degrees of severity of psychotic disorders with some individuals leading a relatively normal life with rare to occasional symptomatic flares. Such episodes have occurred in military aircrew. The short lived psychotic symptoms that occur in aircrew usually are induced by severe stress and or sleep deprivation. Those that last greater than one day but less than 30 days, are usually classified as a brief psychotic disorder or psychotic disorder not otherwise specified (DSM IV).<sup>5</sup>

A form of psychotic disorder that may impact our aircrew members is that associated with alcohol use, substance abuse, prescribed medications, or as a reaction to a medical condition. Psychotic disorders can occur from intoxication from these commonly abused substances: alcohol, amphetamines, cannabis, cocaine, hallucinogens, inhalants, opioids (such as meperidine), phencyclidine, sedatives, hypnotics, and anxiolytics. Similar disorders can occur from withdrawal from these classes of substances: alcohol, sedatives, hypnotics, and anxiolytics. Regarding substance abuse (to include alcohol), it may be difficult to separate primary psychotic disorders from those resulting from substance abuse. There are often some slight differences in the demographics of these two populations that may make it easier to discern the cause. Patients with a substance abuse etiology tend to occur at a later age, have greater antisocial personality disorder comorbidity, higher homelessness, and poorer family support. A flyer's chances of returning to fly after a psychotic episode are far greater if it can be shown that a substance or medication was the cause. For this reason it is of paramount importance to get a good history, a broad laboratory assessment, and a blood alcohol level and a toxicology screen in any aviator who has an episode of psychosis or bizarre behavior.

Treatment for patients with psychotic disorders can be difficult. It may take some time to make a correct diagnosis and these patients are frequently noncompliant with treatment modalities and follow up care. Many of these patients need to be evaluated and treated in a very structured environment with the use of neuroleptic medications. Most of the more serious psychotic disorders

have a significant risk of suicide (and perhaps homicide as well), so this needs to be carefully assessed as well.<sup>7</sup>

### IV. Aeromedical Concerns.

Psychosis is disqualifying for aviation duties. Symptoms of aeromedical concern include poor reality testing, poor insight, eccentric and bizarre behavior, social withdrawal, hallucinations, delusions (sometimes of a persecutory or self-destructive nature), confusion, clouding of consciousness, illogical thought, and a risk of suicide. Because of concern about unpredictable recurrence (with potentially devastating effects upon flying safety, mission completion, and personal health), careful documentation, management, and monitoring are important to aeromedical prognosis. If and when psychosis occurs in an aviator, the flight surgeon must consider waiverable disorders. Potentially waiverable causes of psychosis include toxic (substance-induced psychotic disorder), metabolic, or infectious conditions (psychotic disorder due to a general medical condition), and brief psychotic disorder with marked stressor(s). Thorough documentation during the illness is vital to maximize the probability of an aviator's return to flying status after psychosis. Acute, stress-related psychoses in aviators often resolve quickly with hospitalization and stress relief and without antipsychotic medication

| ICD-9 codes for psychotic disorders |   |  |
|-------------------------------------|---|--|
| 291.3                               | Alcohol-induced psychotic disorder            |  |
| 298.9                               | Unspecified psychosis                         |  |
| 293.9                               | Unspecified Transient Organic Mental Disorder |  |
| 298.8                               | Other and unspecified reactive psychosis      |  |
| 291.8                               | Other specified alcoholic psychosis           |  |
| 291.0                               | Alcohol withdrawal delirium                   |  |

| ICD-10 codes for psychotic disorders |  |  |  |
|--------------------------------------|--|--|--|
| F10.951                              | Alcohol use, unspecified, with alcohol-induced psychotic disorder with |  |  |
|                                      | hallucinations   |  |  |
| F29                                  | Unspecified psychosis not due to a substance or known physiological    |  |  |
|                                      | condition  |  |  |
| F06.8                                | Other specified mental disorders due to known physiological condition  |  |  |
| F23                                  | Brief psychotic disorder   |  |  |
| F10.159                              | Alcohol abuse with alcohol-induced psychotic disorder, unspecified     |  |  |
| F10.231                              | Alcohol dependence with withdrawal delirium                            |  |  |

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| Radiofrequency | Ablation | (RFA) of T | achyarrhy | thmias ( | (Jun ( | 08) |
|----------------|----------|------------|-----------|----------|--------|-----|
|----------------|----------|------------|-----------|----------|--------|-----|

See Catheter Ablation of Tachyarrhythmias and/or Pre-Excitation (WPW)

#### WAIVER GUIDE

Updated: Sep 2015

Supersedes Waiver Guide of Nov 2011

By: Lt Col Kevin D. Hettinger (RAM XVI) and Dr. Dan Van Syoc

Waiver Guide reviewed by Col Matthew Carroll, AF/SG consultant for Rheumatology

## **CONDITION:**

Raynaud's Phenomenom (Sep 2015)

## **III. Waiver Considerations.**

Raynaud's or vasospastic disease is disqualifying for Flying Classes I/IA, II, III and SWA duties. Waiver potential for primary Raynaud's is outlined in the table below. For ATC and GBO personnel and Operational Support Flyers, retention standards state that Raynaud's phenomenon, if frequent, severe, associated with systemic disease or would limit worldwide assignability is disqualifying. Waiver potential for secondary Raynaud's is based on the causal systemic illness or disease process and will be handled on a case by case basis.

Table 1: Waiver potential for primary Raynaud's

| Flying Class | Condition/Treatment             | Waiver Potential   |
|--------------|---------------------------------|--------------------|
| (FC)         |                                 | Waiver Authority** |
| I/IA         | Primary Raynaud's of at least   | Maybe              |
|              | two years duration, infrequent, | AETC               |
|              | requiring no medications        |                    |
|              | Primary Raynaud's requiring     | No                 |
|              | medication                      | AETC               |
| II/III/SWA   | Primary Raynaud's, requiring no | Yes†               |
|              | medications                     | MAJCOM             |
|              | Primary Raynaud's requiring     | Yes†*              |
|              | medications                     | IIA - AFMSA (e.g.  |
|              |                                 | calcium channel    |
|              |                                 | antagonist)        |
|              |                                 | II – MAJCOM (e.g.  |
|              |                                 | ACEi or ARB)       |
| ATC/GBO/OSF  | Primary Raynaud's, requiring no | N/A                |
|              | medications                     |                    |
|              | Primary Raynaud's requiring     | Yes                |
|              | medications                     | MAJCOM             |

<sup>†</sup> Initial waiver duration for primary RP will generally be 2 years. If stability is noted at time of waver renewal, then a 3-year waiver duration is generally appropriate.

<sup>\*</sup> Specifically, coat-core and GITS [Adalat CC® and Procardia XL®, respectively] and amlodipine [Norvasc®]) are the only calcium channel antagonists approved in aviators; they are restricted to non-high performance aviators (FC IIA).

<sup>\*\*</sup> If member does not meet retention standards, waiver authority becomes AFMRA.

A review of AIMWTS in Sep 2015 revealed 35 cases with a diagnosis of Raynaud's. All of the aeromedical summaries were reviewed. Twenty-four cases had primary Raynaud's, 2 cases had secondary Raynaud's, 1 case had Raynaud's secondary to chemotherapy, and 8 cases did not contain enough information to determine if they were secondary versus primary. Thirty of the waiver requests were approved and were either asymptomatic or had very infrequent exacerbations. Five of the 35 cases were disqualified due to uncontrolled RP and other disqualifying diagnoses. Breakdown was as follows: 3 FC I/IA cases (1 disqualified), 15 FC II cases (2 disqualified), 14 FC III cases (2 disqualified), 2 ATC/GBC cases and 1 MOD case.

# II. Information Required for Waiver Submission.

The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The aeromedical summary for initial waiver for RP should include the following:

A. A detailed RP history with attention to inciting factors, frequency, severity and duration of attacks; treatments tried and responses; smoking history; family history of RP and connective tissue diseases. The history should identify factors increasing suspicion for secondary RP as listed above. Pertinent positives as well as negatives should be included. The following three questions should be addressed:

- 1. Are the patient's fingers unusually sensitive to cold?
- 2. Do the patient's fingers change color when they are exposed to cold temperatures?
- 3. Do they turn white, blue, or both?
- B. Thorough physical exam looking for evidence of peripheral vascular disease, peripheral nerve entrapment syndromes, and evidence of diseases associated with secondary RP. A NC should be performed.
- C. Laboratory studies should include: complete blood count, ESR and ANA.
- D. If physical exam or laboratory findings are suggestive of a secondary cause of RP, Rheumatology consultation must be obtained. Additional laboratory studies should include: basic metabolic panel and liver function tests, urinalysis, erythrocyte sedimentation rate, rheumatoid factor, c-reactive protein, complement (C3 and C4), and tests for disease-specific autoantibodies (such as anticentromere antibodies, SCL70 scleroderma and anti-topoisomerase I. Additional waiver criteria for secondary Raynaud's is based on the causal systemic illness or disease process. E. MEB results if required for cases that are frequent, severe, associated with systemic disease or would limit worldwide assignability.

The aeromedical summary for waiver renewal for RP should include the following:

- A. History frequency and severity of attacks; treatment and response; identify factors increasing suspicion for secondary RP.
- B. Physical looking for evidence of peripheral vascular disease, peripheral nerve entrapment syndromes, and evidence of diseases associated with secondary RP. A NC should be performed. C. Laboratories not required unless evidence exists for auto-immune related secondary cause of RP.
- D. Rheumatology consult if evidence exists for auto-immune related secondary cause of RP.

#### III. Overview.

Raynaud's phenomenon (RP), first described by Maurice Raynaud in 1862, is an exaggerated vascular response to cold temperatures or emotional stress. Raynaud's phenomenon (RP) is an exaggerated vascular response of the digital arterial circulation triggered by cold ambient temperature and emotional stress. The diagnosis of RP is based on a history of excessive cold sensitivity and recurrent events of sharply demarcated pallor and/or cyanosis of the skin of the digits. During cold exposure (particularly during shifting temperatures and winter months), Raynaud's attacks increase in frequency and intensity.<sup>1</sup>

Typically, RP presents as episodic attacks that have two distinct phases, an ischemic phase followed by a hyperemic phase. The ischemic phase is noted by well demarcated pallor of the fingers or toes progressing to cyanosis, typically starting in one or several digits spreading symmetrically to all digits. On re-warming, the attack generally ends with rapid reperfusion resulting in erythema (reactive hyperemia). In addition to the vasospastic color changes, other symptoms due to ischemia include pain, paresthesias, numbness, clumsiness of the hand/foot, and potentially ulceration of the skin.<sup>2</sup>

Patients with RP are classified as primary (formerly known as Raynaud's disease) or secondary (formerly known as Raynaud's syndrome). Differentiation between primary RP and secondary RP does not reflect a diagnosis in the strict sense, but rather a description of the current findings in an ongoing screening process. Primary RP describes those RP patients without an underlying disease identified or suspected. Secondary RP describes those RP patients who have a definitively established underlying disease. A third category, suspected secondary RP, is mentioned in the literature and describes those patients with findings suggestive of an underlying disease, such as abnormal nailfold capillaroscopy (NC) or abnormal rheumatologic laboratory testing, but that disease cannot be firmly established at the time of exam.<sup>3</sup> Some underlying diseases associated with secondary RP include scleroderma, mixed connective tissue disease, systemic lupus erythematosus, vasculitis, hematologic abnormalities including cryoglobulinemia, and neurologic disorders including carpal tunnel syndrome. Certain medications (β-adrenergic receptor antagonists, ergot, and amphetamines), trauma, and vibration are also noted secondary RP triggers.<sup>2</sup>

The prevalence of RP estimated through population surveys has ranged between 5-20 percent for women and 4-14 percent for men with significant variation noted between populations studied. Additionally, colder climates have a higher RP burden.<sup>4</sup> A systematic literature review of primary RP found the overall prevalence for primary RP varied from 1.6% to 7.2% in six cross-sectional studies in the general population

(women: 2.1–15.8% and men: 0.8–6.5%), including only studies with clear definition of RP or clear exclusion criteria for secondary RP.<sup>5</sup> A meta-analysis of 10 studies with 640 patients diagnosed with primary RP found that 13% eventually developed a connective tissue disorder (secondary RP).<sup>2</sup>

The diagnosis of the RP is based on the history since there are no simple office tests for cold or emotion induced vasospasm and provocative testing is not recommended.<sup>2</sup> Criteria for the diagnosis of primary RP include vasospastic attacks precipitated by cold or emotional stress, symmetric attacks involving both hands, absence of tissue necrosis or gangrene, no history or physical findings suggestive of a secondary cause, normal NC, normal ESR, and negative

antinuclear antibody test.<sup>4</sup> The likelihood of secondary RP is increased with presence of any of the following features: age of onset > 40 years, male gender, painful severe events with ulceration, asymmetric attacks, RP associated with signs or symptoms of another disease, abnormal labs suggestive of an autoimmune disorder of vascular disease, RP affecting areas proximal to the digits (hand, foot), or abnormal NC with enlarged or distorted capillary loops.<sup>2</sup>

A growing body of literature supports the use of NC in the primary care setting in the workup of RP.<sup>6,7</sup> The use of NC provides the clinician a tool to be used in conjunction with the history and physical exam in discriminating between primary and secondary RP. One study suggests that in patients with RP and negative serologic tests, the presence of giant capillaries (p=0.001), avascular fields (p=0.02), or irregular architecture (p=0.0001) in NC is predictive for the development of a connective tissue disease, mainly scleroderma, CREST, or mixed connective tissue disease.<sup>7</sup>

The technique for NC involves placing a drop of immersion oil on the base of the fingernails of fourth and fifth digits and examining with a handheld ophthalmoscope set at 40+ diopters. The ophthalmoscope is advanced in and out (not touching the oil) until the capillaries are in focus. The normal vascular pattern seen in primary RP and normal vascular control patients consists of a longitudinal linear array of delicate "hairpin" capillary loops while the pattern seen in secondary RP often includes enlarged capillary loops, architectural derangements, and areas of decreased vascularity.<sup>8</sup>

The laboratory evaluation for patients suspected of secondary RP varies based on source cited but generally includes: complete blood count, basic metabolic panel and liver function tests, urinalysis, erythrocyte sedimentation rate, rheumatoid factor, C-reactive protein, complement (C3 and C4), antinuclear antibody, and tests for disease-specific autoantibodies (such as anticentromere antibodies and SCL70 scleroderma antibodies).<sup>2, 9</sup> A rheumatology consultation is also appropriate for suspected secondary RP.

Management of RP is best accomplished by avoidance of cold temperatures and maintenance of total body warmth including the hands and feet. If emotional stress is a contributor, therapies aimed at stress reduction may be of benefit. Avoiding known RP triggers like sympathomimetic drugs, clonidine, and ergotamine is crucial as is avoiding smoking.<sup>4</sup> Pharmacologic management is reserved for poorly controlled/severe RP. Calcium channel blockers are first line therapy with 30 mg of sustained release nifedipine or 5 mg of amlodipine daily recommended. Other classes of medications found beneficial include alpha adrenergic receptor antagonists, topical nitroglycerin, angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor antagonists (ARB), phosphodiesterase inhibitors and selective serotonin reuptake inhibitors. Surgical management focuses on thorascopic sympathectomy and less commonly digital sympathectomy. In each instance recurrence/complication rates were high (82% with the thorascopic sympathectomy and 37% with the digital sympathectomy).<sup>10</sup>

# IV. Aeromedical Concerns.

The major aeromedical concerns associated with a RP episode during flight include sudden subtle incapacitation, distraction and a reduced ability to manipulate cockpit switches. Secondary RP associated with an established underlying connective tissue disease is not compatible with flying. Unavoidable exposure to cold conditions may increase the frequency of episodes and interfere with

the performance of flying duties. This may be a significant factor in determining if the member should be maintained in the aviator status.

Calcium channel antagonists (specifically coat-core and GITS [Adalat CC® and Procardia XL®, respectively] and amlodipine [Norvasc®]) are approved in aviators; they are restricted to non-high performance aviators.

| ICD-9 Code for Raynaud's phenomenon |  |  |
|-------------------------------------|--|--|
| 443.0                               | Raynaud's syndrome/disease               |  |
| 443.9                               | Peripheral vascular disease, unspecified |  |

| ICD-10 Code for Raynaud's phenomenon |  |  |
|--------------------------------------|--|--|
| I73.00                               | Raynaud's syndrome without gangrene      |  |
| I73.9                                | Peripheral vascular disease, unspecified |  |

## V. References.

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## Refractive Error, Excessive (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: New Ground Based Operator (GBO) Standards. MSD C TABLE ONE.

## I. Waiver Consideration

Refractive errors standards are listed in Section C, TABLE ONE of the Medical Standards Directory for all flying classes and special operational duty. Excessive refractive error is not listed specifically as disqualifying for ATC, GBO (RPA SO and MOD), and SWA duties. Members must correct to 20/20 in each eye at distance and near for ATC and SWA duties. Members must correct to 20/20 in the better eye and 20/400 in the worse eye for GBO. SWA personnel must also meet sister service standards IAW AR40-501 and NAVMED 15-102/105.

The following tables cover the different flying classes, waiver potential, and ACS review/evaluation for myopia, hyperopia, astigmatism, and anisometropia. If refractive errors are greater than those listed in the tables below for FC I/IA, no waiver will be granted.

Table 1: Myopia

| Flying Class        | Refractive error | Waiver    | Waiver Authority | ACS               |
|---------------------|------------------|-----------|------------------|-------------------|
|                     |                  | Potential |                  | review/evaluation |
| FC I                | > -3.00          | No        | AETC             | No                |
| FC IA               | > -4.50          | No        | AETC             | No                |
| FC II(non-pilot)/FC | > -5.50          | Yes       | AETC             | No                |
| III/GBO (RPA Pilot) |                  |           |                  |                   |
| ATC/GBO (RPA        | N/A              | N/A       | N/A              | N/A               |
| SO/MOD)             |                  |           |                  |                   |
| SWA                 | > -8.00          | No        | AETC/Army/Navy   | No                |

Table 2: Hyperopia

| Flying Class        | Refractive error                | Waiver<br>Potentia | Waiver<br>Authority | ACS<br>review/evaluati |
|---------------------|---------------------------------|--------------------|---------------------|------------------------|
|                     |                                 | 1                  |                     | on                     |
| FC I                | $> +2.00 \text{ but} \le +3.00$ | Yes                | AETC                | Yes                    |
|                     | $> +3.00 \text{ but} \le +4.00$ |                    |                     |                        |
| FC IA               | $> +3.00 \text{ but} \le +4.00$ | Yes                | AETC                | Yes                    |
|                     | $> +4.00 \text{ but} \le +5.50$ |                    |                     |                        |
| FC II(non-pilot)/FC | > +5.50 1                       | Yes                | AETC                | Maybe <sup>3</sup>     |
| III                 |                                 |                    |                     |                        |
| GBO (RPA Pilot)     | >+5.50                          | Yes                | AETC                | Yes                    |
| ATC/GBO (RPA        | N/A                             | N/A                | N/A                 | N/A                    |
| SO/MOD)             |                                 |                    |                     |                        |
| SWA                 | >+8.00                          | No                 | AETC/Army/Nav       | No                     |
|                     |                                 |                    | у                   |                        |

<sup>1.</sup> If waiverable degradation in stereopsis, (meets waiver criteria for defective depth perception, see waiver guide on stereopsis), then waiver potential exists.

**Table 3: Astigmatism** 

| Flying Class    | Refractive | Waiver    | Waiver    | ACS               |
|-----------------|------------|-----------|-----------|-------------------|
|                 | Error      | Potential | Authority | review/evaluation |
| FC I/IA         | >3.00      | No        | AETC      | No                |
| FC II/FC III    | >3.00      | Yes       | AETC      | Yes               |
| GBO (RPA Pilot) |            |           |           |                   |
| ATC/GBO (RPA    | N/A        | N/A       | N/A       | N/A               |
| SO/MOD)/SWA     |            |           |           |                   |

Table 4: Anisometropia

| Flying Class       | Refractive         | Waiver    | Waiver    | ACS               |
|--------------------|--------------------|-----------|-----------|-------------------|
|                    | Error <sup>1</sup> | Potential | Authority | review/evaluation |
| FC I               | > 2.00             | Yes       | AETC      | Yes               |
| FC IA              | > 2.50             | Yes       | AETC      | Yes               |
| FC II(non-pilot/FC | > 3.50             | Yes       | AETC      | No                |
| III                |                    |           |           |                   |
| GBO (RPA Pilot)    |                    |           |           |                   |
| ATC/GBO (RPA       | N/A                | N/A       | N/A       | N/A               |
| SO/MOD)/SWA        |                    |           |           |                   |

<sup>1.</sup> If normal stereopsis or waiverable degradation in stereopsis and no asthenopic symptoms or diplopia. Waiverable degradation of stereopsis means meets waiver criteria for defective depth perception (see waiver guide on subject).

<sup>2.</sup> If no degradation in stereopsis, then waiver potential exists.

<sup>3.</sup> Hyperopes with defective depth perception may be referred to the ACS at the discretion of the waiver authority.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# Myopia

## A. Initial Waiver Request:

- 1 Cycloplegic refraction (Initial FC II/III/GBO-RPA Pilot) to 20/20 each eye and manifest refraction to best corrected visual acuity each eye.
- 2 Optometry/ophthalmology exam to include a dilated peripheral retina exam of each eye.
- 3 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# Hyperopia

# A. Initial Waiver Request:

- 1. Cycloplegic refraction (FC I/IA and initial FC II/III/GBO-RPA Pilot) to 20/20 each eye and manifest refraction to best corrected visual acuity each eye.
  - 2. Stereopsis testing (OVT).
  - 3. Optometry/ophthalmology exam to include:
    - a. Ductions, versions, cover test and alternate cover test in primary and 6 cardinal positions of gaze.
    - b. AO Vectograph stereopsis and suppression tests at 6 meters
    - c. Randot or Titmus stereopsis test (near stereopsis tests).
    - d. Red lens test.
    - e. Four-diopter base-out prism test at 6 meters.
    - b. History of asthenopic (eye pain/fatigue) symptoms, diplopia.
    - c. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# **Astigmatism**

## Initial Waiver Request:

- 1. Cycloplegic refraction (Initial FC II/III/GBO-RPA Pilot) to 20/20 each eye and manifest refraction to best corrected visual acuity each eye.
- 2. Corneal topography imaging. All corneal topography (CT) submissions should be formatted in **Axial** view using a standard dioptric scale (39.0 to 50.0 Diopter range, 0.50 Diopter increments) and standard color palette. The **OD/OS Display** with an **Axial Map** and an **Axial Numeric View** is preferred. All ATLAS topographies should display the **Axial I-S** value.
- 3. Corrected visual acuity with spectacles, and contact lenses if applicable, each eye.
- 4. Corrected low contrast acuity (PV 5% chart) with spectacles, and contact lenses if applicable, each eye.
- 5. Stereopsis testing (OVT).
- 6. Optometry/ophthalmology exam to include slit lamp and fundus exam.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# Anisometropia

# Initial Waiver Request:

- 1. Cycloplegic refraction (FC I/IA and initial FC II/III/GBO-RPA Pilot) to 20/20 each eye and manifest refraction to best corrected visual acuity each eye.
- 2. Stereopsis testing (OVT).
- 3. Optometry/ophthalmology exam to include:
  - a. Ductions, versions, cover test and alternate cover test in primary and 6 cardinal positions of gaze.
  - b. AO Vectograph stereopsis and suppression tests at 6 meters
  - c. Randot or Titmus stereopsis test (near stereopsis tests).
  - d. Red lens test.
  - e. Four-diopter base-out prism test at 6 meters.
  - 7. History of asthenopic (eye pain/fatigue) symptoms, diplopia or fusional problems, to include negative responses.
  - 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

**Note:** For all FC I/IA applicants, confirmation that individual has discontinued wear of soft contacts for at least 30 days or hard/rigid gas permeable contact lenses for at least 90 days at the time of exam is required.

#### III. Aeromedical Concerns

Aeromedical refractive error is based on the cycloplegic refraction for all initial flying class exams. The authorized cycloplegic exam technique uses 1% cyclopentolate (Cyclogyl), 2 drops each eye, 5 to 15 minutes apart, with examination performed no sooner than one hour and no later than two hours after the second drop. The cycloplegic refractive error is the minimum refractive power needed to achieve 20/20 visual acuity in each eye. The refractive error standard for aeromedical purposes is that produced following transposition. The rules of transposing are: (1) <u>Algebraically</u> add the cylinder power to the sphere power to determine the transposed power of the sphere (2) Change the sign of the cylinder (3) Change the axis by 90 degrees (do not use degrees greater than 180 or less than 0). Note: 180 degrees is used in place of 0 degrees.

|            |       | Sphere | Cylind | er  | Axis |
|------------|-------|--------|--------|-----|------|
| Example 1: | -0.75 | -1.00  | X      | 179 |      |
| Transposed | -1.75 | +1.00  | X      | 089 |      |
| Example 2: | -4.25 | -1.25  | X      | 068 |      |
| Transposed | -5.50 | +1.25  | X      | 158 |      |

By transposing a refractive error, the most plus and most minus meridians can easily be determined. In example 1, -0.75 is the most plus meridian and -1.75 is the most minus meridian. When applying aeromedical standards and waiver criteria, both of these values must fall within the allotted range based on the flying class. If the candidate in example 1 was applying for FCI, Table One of the Medical Standards Directory (MSD) would show that the most plus meridian can be no greater than

+2.00 and the most minus meridian can be no less than -1.50. Graphically, this would be represented as shown below, and it is apparent that this refraction would exceed the standard for myopia.



Astigmatism may be represented by either a positive or negative cylinder value depending on the axis referenced. When applying aeromedical standards and waiver criteria, the sign of the value is irrelevant as the physical meaning of astigmatism is simply a difference between two points.

Improper or unbalanced correction with spectacles or contact lens can degrade stereopsis and contrast sensitivity as well as induce generalized ocular pain and fatigue (asthenopia). Myopia is more likely to progress, with respect to the degree of myopia, regardless of age, while hyperopia tends to remain static over time. In addition, myopes may see halos or flares around bright lights at night and are also at risk for worsening vision under dim illumination and with pupil enlargement, a phenomena known as "night myopia." Myopes also have an increased risk of retinal detachment, open angle glaucoma and retinal degenerations, such as lattice.

Hyperopes, especially those with greater than +3.00 D of correction, will experience greater problems with visual acuity after treatment with atropine or topical cycloplegic agents. They have a greater predisposition for tropias, microstrabismus, and phorias that can decompensate under the rigors of flight. They also have a higher prevalence for amblyopia due to the accommodative esotropia and anisometropia. Moreover, hyperopes have more problems with visual aids, such as night vision goggles, as they develop presbyopia at earlier ages compared to myopes. Lastly, hyperopes are more likely to develop angle closure glaucoma than myopes.

Higher levels of astigmatism or progressive astigmatism can be associated with potentially progressive corneal conditions, such as keratoconus, that can degrade image quality and visual performance during productive years of flying career. Anisometropias have greater association with diplopia, fusional discrepancies (e.g. defective stereopsis), and amblyopia, especially when greater than 2.00 D refractive error difference between the two eyes.

In general, corrective measures presently available to correct refractive errors include spectacles, contact lenses, and corneal refractive surgical techniques such as PRK, LASIK, and ICL implantation. Spectacles impose an additional optical interface between the aircrew's eyes and the outside world. This increases the risk of internal reflections, fogging, as well as reduction in the light reaching the retina leading to visual distortion. These phenomenon are especially more common in high myopes and in higher levels of astigmatism. Finally, spectacle frames interfere with the visual field, cause potential hot spots, and displace under G forces. Depending on nature and magnitude of the refractive error, the lenses themselves can induce optical blind spots (scotomas), optical image size changes, and can create unacceptable effects on other visual performance parameters, such as stereopsis. Contact lenses share some of these same problems, but reduce some of the drawbacks of spectacles, such as changes in image size, peripheral vision interference, hot spots from frames, fogging, and blind spots. However, contact lenses introduce

their own unique aeromedical problems particularly related to maintenance and wear. In addition, further concern exists with the risk of acutely having to perform without the corrective lenses, such as after spontaneous lens loss, e.g. after ejection or during a deployment without adequate backups. See corneal Refractive Surgery and Implantable Collamer Lens Waiver Guides for further discussion on advantages and risks of refractive surgery.

AIMWTS review of each of these four diagnoses produces a large number of cases. In 2015, there were 8420 cases of myopia, 496 cases of hyperopia, 2079 cases of astigmatism and 153 cases of anisometropia. It is no longer necessary to do new searches that will produce even larger numbers. These are common diagnoses in the aviation population, but it is important that we continue screening our aviators for quality of vision.

| ICD-9 Codes for Refractive Errors |               |
|-----------------------------------|---------------|
| 367.0                             | Hyperopia     |
| 367.1                             | Myopia        |
| 367.2                             | Astigmatism   |
| 367.31                            | Anisometropia |

| ICD-10 Codes fo | ICD-10 Codes for Refractive Errors          |  |  |
|-----------------|---|--|--|
| H52.0           | Hypermetropia, right, left, both            |  |  |
| 1, 2, 3         |   |  |  |
| H52.1           | Myopia, right, left, both                   |  |  |
| 1, 2, 3         |   |  |  |
| H52.20          | Unspecified astigmatism, right, left, both, |  |  |
| 1, 2, 3, 9      | unspecified                                 |  |  |
| H52.31          | Anisometropia                               |  |  |
| H52.7           | Unspecified disorder of refraction          |  |  |

# IV. Recommended Readings

No external references were used in producing this waiver guide.

# **Refractive Surgery (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (ACS Ophthalmology Branch Chief), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** Slit lamp exam results returned to Table 2 and clarification added to Section I that steroid eye drops used to treat or prevent inflammation after approved CRS do not result in DNIF. Underlying condition requiring the use of steroid drops may require DNIF. New Ground Based Operator (GBO) Standards. MSD C33, C34.

## I. Waiver Consideration

Uncomplicated Refractive Surgery is not disqualifying for all classes of flying duties and Aviation and Aviation Related Special Duty (AASD) if pre-refractive Surgery Cycloplegic refractive error limits were met (Table 3). Waiver is required only if complications occurred or if surgery was performed beyond the standards but does not exceed waiver limits (Table 4). Members who don't require a waiver are managed locally with a DNIF and may return to flying duties once cleared by the flight surgeon, co-managing optometrist, and surgeon (if needed). All LASIK flap dislocations need to be evaluated in person at the ACS even if treated promptly and deemed healed by the treating ophthalmologist. There is a risk in such cases of quality of vision deficits. Return to Flying Duties/Waiver may be initiated as early as 30 days postop for LASIK and 6 weeks postop for PRK if the surgery and/or complication has been managed appropriately with return of good visual acuity (Table 2).

For ATC, GBO and SWA personnel, a history of refractive surgery is only disqualifying if the surgical outcome results in the member's inability to meet visual standards for the career field.

Steroid eye drops used to treat or prevent inflammation after approved CRS do not automatically lead to DNIF. The member should remain DNIF until cleared by flight surgeon, optometrist, and surgeon once the member meets vision standards, and is deemed clear, as outlined in Table 2. Members may need anti-inflammatory drops after they have been deemed clear to return to flight status, but do not need to be DNIF during the rest of their time using these drops.

**Table 1: Waiver potential for Refractive Surgery with Complications** 

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation |
|-------------------|------------------|------------------|--------------------------|
| I/IA              | Yes              | AETC             | Yes                      |
| II/III            | Yes              | MAJCOM           | Yes                      |
| ATC, GBO, SWA     | Yes              | MAJCOM           | Yes                      |

Table 2: Vision Standards for Return To Flying Duties or to Initiate Waiver (if required)

| Examination                            | Waiverable Results                             |
|--|--|
| Best corrected visual acuity (OVT)     | 20/20 or better each eye                       |
| Precision Vision 5% low contrast chart | 20/50 or better each eye                       |
| Refractive error                       | Stable, no more than 0.50 diopter shift in     |
|  | manifest sphere or cylinder refractive power   |
|  | between two readings at least 2 weeks apart    |
| Slit lamp exam                         | LASIK – no visually significant striae or flap |
|  | complications                                  |
|  | PRK – no visually significant corneal haze     |
| Fundus exam                            | No new or previously unrecognized retinal      |
|  | pathology                                      |
| Depth perception (OVT-DP)              | Line B or better. If fails, refer to defective |
|  | depth perception/stereopsis waiver guide.      |

**Table 3: Pre-RS Cycloplegic Refractive Error Limits (AASD)** 

| Myopia (Most myopic meridian)       | ≤ -8.00 Diopters |
|-------------------------------------|------------------|
| Hyperopia (Most hyperopic meridian) | ≤ +3.00 Diopters |
| Astigmatism                         | ≤ 3.00 Diopters  |

Table 4: Pre-RS Cycloplegic Refractive Error Limits (Exceeds AASD and Requires Waiver)<sup>1</sup>

| Refractive Error          | <b>Untrained Applicants</b> | Trained Applicants |
|---------------------------|-----------------------------|--------------------|
| Myopia (Most myopic       | $\leq$ -10.00 Diopters      | ≤ -10.00 Diopters  |
| meridian)                 |                             |                    |
| Hyperopia (Most hyperopic | ≤ +5.00 Diopters            | ≤ +4.00 Diopters   |
| meridian)                 |                             |                    |
| Astigmatism               | ≤ 6.00 Diopters             | ≤ 3.00 Diopters    |

<sup>1.</sup> Applicant/Member may not qualify for a waiver for surgery in excess of AASD standards unless member had a good outcome and is able to meet other vision standards. Special warfare airmen must meet sister service standards while training with sister services.

**Table 5: USAF Corneal Refractive Surgery Clinical Guidelines (AADS CRS Program and Standards)** 

| ·                                |  | PRK <sup>8, 9</sup>                                   | LASIK <sup>7, 9</sup>                                 | Hyperopia <sup>6,9</sup>                           |
|----------------------------------|--|---|---|--|
|                                  |  | Plano to ≤ -<br>8.00                                  | <b>Plano to ≤ -8.00</b>                               | <b>Plano to ≤ +3.00</b>                            |
|                                  | Surgery  | Any DoD RS<br>Center/Civilian <sup>1</sup>            | Any DoD RS<br>Center/Civilian <sup>1</sup>            | Any DoD RS<br>Center/Civilian <sup>1</sup>         |
| Trained<br>Aircrew               | 1-year post-<br>op exam                          | Local Eye<br>Clinic/Civilian <sup>1</sup>             | Local Eye<br>Clinic/Civilian <sup>1</sup>             | Local Eye<br>Clinic/Civilian <sup>1</sup>          |
|                                  | Waiver<br>Authority <sup>5</sup>                 | MAJCOM  | MAJCOM  | MAJCOM   |
|                                  | Surgery  | USAFA/Civilian<br>& Any DoD RS<br>Center <sup>1</sup> | USAFA/Civilian &<br>Any DoD RS<br>Center <sup>1</sup> | USAFA/Civilian &<br>Any DoD RS Center <sup>1</sup> |
| Pilot<br>Applicants <sup>2</sup> | Exam requirement for initial waiver <sup>3</sup> | USAFA/ACS at time of MFS                              | USAFA/ACS at time of MFS                              | ACS <sup>4</sup> /ACS at time of MFS               |
|                                  | Waiver<br>Authority                              | AETC  | AETC  | AETC <sup>4</sup>                                  |
| RPA Pilot                        | Surgery  | Any DoD RS<br>Center/Civilian <sup>1</sup>            | Any DoD RS Center/Civilian <sup>1</sup>               | Any DoD RS<br>Center/Civilian <sup>1</sup>         |
| Applicants                       | Initial follow-up for waiver                     | Local Eye<br>Clinic/Civilian <sup>1</sup>             | Local Eye<br>Clinic/Civilian <sup>1</sup>             | USAFA/ACS at time of MFS                           |

- 1. If not eligible for TRICARE medical benefit (e.g. civilian, ROTC & most ANG/AFRC), will go to civilian provider.
- 2. AD pilot applicants are considered Warfighters until selected for training [they must have a qualified physical exam (pending MFS) <u>before</u> selection]. They must meet the AASD or waiver criteria.
- 3. Post-op exam for initial FC I application must be at least six months after date of surgery (e.g. history of PRK or LASIK no sooner than six months ago). Applicants must be one year after surgery for hyperopic treatments.
- 4. For USAFA cadets, ACS review/evaluation is required prior to waiver (no "contingent on MFS" waivers) if there was a complication.
- 5. Waiver authority for initial and renewal, if the surgery was in excess of AASD standards and/or complications were experienced.
- 6. For both PRK and LASIK.
- 7. Members who have LASIK should have a minimum two-week DNIF period, however, up to 1 month may be required to fully stabilize following LASIK. Initial waiver can be requested once applicable vision standards are met and refractive stability is established if the surgery was in excess of AASD standards and/or there was a complication.
- 8. Members who have PRK should have a minimum two-week DNIF period, however, 2-3 months is generally required for enough corneal healing to occur to meet applicable vision standards and for refractive stability to occur.
- 9. All initial waivers must meet other set vision standards and meet the waiver criteria in Table 4 above.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations. Waiver potential and waiver limits are outlined in Tables 1, 2, 3, and 4. The essential elements of the USAF Refractive Surgery Program are outlined in Table 5 above.

If the <u>trained aircrew member</u> has an uncomplicated postoperative course, meets applicable vision standards, and met pre-refractive cycloplegic refractive error limits in Table 3, member may resume flying duties once cleared by their flight surgeon, co-managing optometrist, and surgeon (if necessary). All follow-up appointments, including the 12-month post op evaluation should still be accomplished to meet RS standard of care requirements. Annual routine PHA vision exams will be required after this point. Complicated cases, cases that exceed AASD standards, or cases not meeting vision standards post-operatively should be referred to the ACS for review.

While on anti-inflammatory (steroid) eye drops, the aviator will be placed on non-mobility status, restricting the individual from deployment via AF Form 469. For LASIK, the aircrew member will similarly be placed on non-mobility status, restricting the individual from deployment via AF Form 469 for a minimum of one month after surgery, even if no longer on steroid eye drops.

Any complications that arise will require waiver after the complication is successfully managed.

## A. <u>Initial Waiver Request for **trained** AASD members:</u>

- 1. History
  - a. Pre-op cycloplegic refraction.
  - b. Surgical procedure, date, location, complication, and management of the complication.
  - c. Assessment (negative and positive) of post-op symptoms of glare, halos, reduced night vision and diplopia.
  - d. Eye medications usage, past and current, include discontinuation date.
- 2. Physical (current):
  - a. Uncorrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
  - b. Best corrected visual acuity high contrast (OVT) and Precision Vision 5% low contrast.
  - c. Cycloplegic refraction and dilated fundus exam.
  - d. Two post-op refractions at least 2 weeks apart that shows stability (no more than 0.50 diopter shift in **manifest** sphere or cylinder power).
  - e. Slit lamp exam, which must include grading of haze, if present.
  - f. Intraocular pressures (IOPs).
  - g. Depth perception (OVT-DP). (If fails and previously waived for defective depth perception using AO Vectograph, then include AO Vectograph).
- 3. Attach copy of "Permission to Proceed" letter.
- 4. Attach copy of the operative report for each eye treated, post-RS evaluations (1, 3, 6, 12 months post-op and annually, and any other additional follow-ups) and any RS-related incidents (this will meet the requirement to send this info to the USAF-RS APM). The following is a link to the post-RS evaluation form to be utilized: <a href="https://kx.health.mil/kj/kx1/AFRefractiveSurgery/Pages/home.aspx">https://kx.health.mil/kj/kx1/AFRefractiveSurgery/Pages/home.aspx</a> or <a href="https://kx.health.mil/kj/kx1/AFRefractiveSurgery/Documents/Forms/ShowFolders.aspx?RootFolder=/kj/kx1/AFRefractiveSurgery/Documents/New%20CRS%20PDF%20forms&FolderCTID=0x01200042E4CD4D09D1524EB5B8D337F9AD1615&View=%7bD5DE7241-B6EB-4E3D-A94E-D3E74D33084D%7d</a>
- 5. If any of the above requested items cannot be provided, please provide an explanation to the waiver authority in the AMS why that could not be provided.

# B. <u>Initial Waiver Request for **untrained** AASD applicants:</u>

- 1 History/Physical:
  - a. Address whether all clinical criteria prior to RS were met. If not, describe exceptions in detail.
  - b. Description of other surgical or post-operative complications (e.g. corneal haze, flap striae, ocular hypertension, etc.)
  - c. Must be 6 months post-RS, at minimum, for application consideration (one year for hyperopic treatments).
  - d. All other items required for History and Physical for trained AASD members above in section A.
  - Attach copy of the operative report for each eye treated, post-RS evaluations and any RS-related incidents (this will meet the requirement to send this info to the APM. The following is a link to the post-RS evaluation form which should be used:
  - https://kx.health.mil/kj/kx1/AFRefractiveSurgery/Pages/home.aspx or https://kx.health.mil/kj/kx1/AFRefractiveSurgery/Documents/Forms/ShowFolders.aspx?Rootfolder=/kj/kx1/AFRefractiveSurgery/Documents/New%20CRS%20PDF%20forms&FolderCTID=0x01200042E4CD4D09D1524EB5B8D337F9AD1615&View=%7bD5DE7241-B6EB-4E3D-A94E-D3E74D33084D%7d
- 2 Initial waiver term of validity may be indefinite at the waiver authority's discretion; however, AASD applicants are not eligible for waiver until the complication has been managed and member has stabilized and otherwise meets vision standards. Post-RS evaluations are desired at 1, 2 (if PRK), 3, 6, and 12 months post-op. All examination documentation obtained to date is required for submission for the initial waiver.
- 3 If any of the above requested items cannot be provided, please provide an explanation to the waiver authority in the AMS why that could not be provided.

#### III. Aeromedical Concerns

These elective surgical procedures, although highly successful in general, are not risk free and represent an investment by the patient and his/her squadron initially. Topical steroids are required following RS to control the healing response and reduce the risk of corneal haze and scarring. However, topical steroids may increase the risk of infection, produce elevated intraocular pressure in some individuals, and may cause development of cataracts. To date, two aircrew members have sustained permanent visual field defects and vision loss because of topical steroid related complications. Therefore, frequent monitoring of intraocular pressure and close follow-up is required.

AASD personnel are restricted from deployment as long as steroid eye drops are in use; however, if waiver required, the aircrew member may be waived by the MAJCOM waiver authority to return to local flight duties in order to maintain qualifications. Participation in flight simulator and altitude chamber training while on steroid eye drops is permissible after initial waiver is granted by the waiver authority. An aeromedical summary submitted to MAJCOM waiver authority must provide evidence that all applicable vision standards are met, any post-operative complications have resolved, and the refraction is stable (two refractions separated by at least two weeks with no more than 0.50D change.) When the aviator has been directed to discontinue steroid eye drop use, the member may be returned to world-wide-qualified status for deployment purposes.

Degradation in the quality of vision following RS can affect operational visual performance, despite a finding of high contrast visual acuity (standard vision charts) that meets flight standards. Significant complications include dry eye symptoms, corneal haze, glare, halos, diplopia, reduced low contrast sensitivity, unaided night vision, and night vision goggles (NVG) performance. Recovery from RS complications may require extended recuperation time extending to a year or more. Under- and over-corrections of refractive errors can result from both PRK and LASIK treatments. Refractive surgery enhancement (secondary treatment) or requirement to wear traditional correction (spectacles or contact lenses) may be required. UV protection is required post-RS to reduce UV-induced phototoxic damage than can potentiate corneal haze.

LASIK procedures uniquely present flap complication risks. Intra-operative complications, while rare, include thin flap, incomplete flap, buttonhole flap or free flap. In addition, flap striae (wrinkles) can develop intra-operatively or at any time during the convalescent period. Surgical intervention is usually required to address striae complications if visual acuity is affected. The risk of corneal flap displacement by high Gz forces or ejection sequences is low. The effect of chronic, low-grade hypoxia on visual performance following LASIK has not been completely studied. A single study at sea level (normobaria) with simulated hypoxic environment equivalent to 25K feet revealed no reduction in vision. The effects of altitude up to 35K feet in an aviation environment following both PRK and LASIK has been studied with no adverse effects noted. Infectious keratitis can occur during the immediate postoperative period, which can be vision threatening. Best-corrected visual acuity may decrease by two or more lines in up to 3.6% of patients if keratitis occurs.

Flight surgeons should encourage post-RS aircrew to prepare for long duration flights and pending deployments. A bottle of sterile lubricating eye drops assists aviators in managing dry eye symptoms (a common post-RS complication) and thus minimizes rubbing of the eyes, which can precipitate corneal abrasions or LASIK flap dislocation. Post-operatively, aircrew must continue to be alert and vigilant in the use of eye protection in both operational and recreational environments, especially after LASIK.

Recently, a change was made to allow waivers for members in excess of AASD limits (Table 4). This change was recommended based on nearly two decades of success of the USAF refractive surgery program as well as numerous studies showing the continued safety of the procedures. For myopia, the most feared complication is that of retinal tears and retinal detachment. A retrospective review of 1554 eyes who underwent LASIK for refractive error between -8.00 to -27.50 showed only four retinal detachments (0.25%). The rate of retinal detachment in aircrew in the excessive myopia management group (members who had refractive surgery from -5.50 to -8.00 diopters) was found to be 0.08% and was 0.22% for retinal tears. With hyperopic treatments, the concern is the quality of vision and risk of regression. Current literature on modern laser platforms show 86% of eyes +0.50 to +8.50 have best corrected acuity of 20/20 one year after procedure and there is a 2.13% loss of two lines or more of best corrected visual acuity. Another study looking at a sixth generation laser platform found outcomes to be very stable with regression of only 0.14 diopters reported over a one year period. Therefore, even in more extreme refractive errors, it does seems reasonable to offer refractive surgery, especially as these are the members with the most to gain from having surgery.

A waiver may be granted by the waiver authority at initial waiver following **complicated approved refractive surgery or uncomplicated surgery in excess of AASD limits** once the aircrew member is off all medications and meets post-op stability and vision criteria.

| ICD-10 Co  | ICD-10 Codes for Corneal Refractive Surgery             |  |  |
|------------|---|--|--|
| H52.0      | Hypermetropia, right, left, both                        |  |  |
| 1, 2, 3    |   |  |  |
| H52.1      | Myopia, right, left, both                               |  |  |
| 1, 2, 3    |   |  |  |
| H52.20     | Unspecified astigmatism, right, left, both, unspecified |  |  |
| 1, 2, 3, 9 |   |  |  |
| 08Q8XZZ    | Repair right cornea, external approach                  |  |  |
| 08Q9XZZ    | Repair left cornea, external approach                   |  |  |

## **IV. Suggested Readings**

- 1. Larys RP. LASIK at high altitude a study of the worst-case mission scenario. Presented at the International Military refractive Surgery Symposium, February 5-7, 2007 in San Antonio, Texas.
- 2. Tutt RC, Baldwin JB, Ivan DJ, et al. Simulated altitude and G-force tolerance after photorefractive keratectomy (PRK). Brooks City Base, TX: USAF School of Aerospace Medicine; 2005 June. Report No: SAM-FE-BR-TR-2005-0002.
- 3. Aaron M, Wright S, Gooch J, et al. Stability of Laser-Assisted In Situ Keratomileusis (LASIK) at Altitude. Aviat Space Environ Med, 2012; 83: 958-61.
- 4. Ruiz-Moreno JM, Perez-Santonja, JJ, and Alio JL. Retinal Detachment in Myopic Eyes After Laser In Situ Keratomileusis. Am J Ophthalmol, 1999; 128(5):588-594.
- 5. Sandoval HP, Donnenfeld ED, Kohnen T, et al. Modern Laser In Situ Keratomileusis Outcomes. J Cataract Refract Surg 2016; 42:1224-1234.
- 6. Gharaibeh Villanueva A, Mas D, et al. Corneal Stability Following Hyperopic LASIK with Advanced Laser Ablation Profiles Analyzed by a Light Propagation Study. J Ophthalmol, vol. 2018, Article ID 3060939, 10 pages, 2018.

#### WAIVER GUIDE

Updated: Jul 2014

Supersedes Waiver Guide of Jun 2010

By: LT Ajiri Ikede (RAM XV), Maj Amy Gammill (ACS Internal Medicine Branch) and Dr. Dan Van

Syoc

Reviewed by Lt Col Timothy Phillips, AF/SG consultant for Urology

#### **CONDITION:**

Renal and Ureteral Stones (Nephrolithiasis) (Jul 2014)

#### I. Waiver Considerations.

Recurrent renal stones are disqualifying for all flying classes in the US Air Force. No waiver is required for a single episode in a <u>trained aviator unless retained stones are present</u>. However, a full metabolic workup is required after a single episode of nephrolithiasis. Following a recurrent episode, pilots need to be stone-free for waiver consideration unless they fly with another trained pilot; a restricted waiver (FC IIC) is considered for them if they are asymptomatic, particularly if they have 3 or less stones that are <4 mm in size. These aviators are typically followed every 6-12 months for a change in the size of the calculus, and if stable over a year, annual follow-up is deemed safe. The same protocol is followed for asymptomatic stones found incidentally on imaging studies. In all instances, metabolic risk factors for stone disease must be appropriately addressed before waiver will be considered.

Table 1: Waiver criteria for renal stones

| Flying Class | Category                 | Waiver Potential        |
|--------------|--------------------------|-------------------------|
|              |                          | Waiver Authority        |
| I/IA         | Single episode           | No waiver required, but |
|              |                          | full workup required on |
|              |                          | FC I/IA physical.       |
|              | D (12) ( 1               | NT                      |
|              | Recurrent, bilateral, or | No                      |
|              | retained                 | AETC                    |
| II**         | Recurrent or bilateral#  | Yes                     |
|              |                          | MAJCOM                  |
|              | D . 14//                 | 37                      |
|              | Retained*#               | Yes                     |
|              |                          | MAJCOM                  |
| III/SWA**    | Recurrent or bilateral   | Yes                     |
|              |                          | MAJCOM                  |
|              | Retained*                | Maybe                   |
|              | Retained                 | MAJCOM                  |
| ATC/CDO**    | Degrament on hilotonal   |                         |
| ATC/GBO**    | Recurrent or bilateral   | Yes                     |
|              |                          | MAJCOM                  |
|              | Retained*!               | Maybe                   |
|              |                          | MAJCOM                  |

<sup>\*</sup>Stone in renal parenchyma or cyst, with no possibility of movement into collecting system, waiver likely for trained asset.

AIMWTS review from Jan 2011 through Jul 2014 revealed 505 submitted cases for stone disease; 45 resulted in a disqualification. Breakdown of the cases revealed: 10 FC I/IA cases (6 disqualified), 234 FC II/IIC cases (5 disqualified), 213 FC III cases (29 disqualified), 42 ATC/GBC cases (4 disqualified), and 6 MOD cases (1 disqualified). Rationale for disqualifications included frequency and severity of renal colic as well as the size and location of retained stones. In addition, disqualification decisions were made on the basis of the presence of other serious comorbidities that when taken together with the history of nephrolithiasis, would render the aeromedical risk to be intolerable.

# II. Information Required for Waiver Submission.

## Information required for an initial waiver:

A. Complete history to include possible etiologic events; attempts to catch the stone, number and size of any stones, and complete work-up done at the time of the episode. Report any history of episodes prior to going on flying status. Is there family history of stones or personal history of gout, low fluid intake, high animal protein intake, high salt intake, low calcium intake or use of vitamin D supplements? History of all medications used, prescription and over-the-counter, is also necessary.

<sup>#</sup> If flyer is a pilot, and there are any retained stones, then FC IIC and AFMSA is waiver authority.

<sup>\*\*</sup> Untrained FC II, III, ATC/GBO, and SWA personnel should be viewed is same manner as FC I/IA.

<sup>!</sup> Retained renal stones not disqualifying for GBO personnel.

- B. Labs: Stone analysis; urinalysis, including urine pH and urine culture; one complete 24-hour urine assessment should be done while on patient's usual diet for urine volume, calcium, oxalate, uric acid, citrate, magnesium, phosphorus, urine sodium, and creatinine excretion; serum electrolytes, blood urea nitrogen (BUN), serum creatinine, calcium, phosphate, and uric acid; and parathyroid hormone level. Urine creatinine is measured to determine the adequacy of urine collection.
- C. Imaging studies: baseline KUB required. If non-contrast CT, IVP, or ultrasound obtained, these study reports must also be submitted with the AMS.
- D. Urology consult addressing treatment and if retained stones present, addressing likelihood of stone entering the collecting system. Successful pursuit of a waiver may be expedited by referring the patient early to an Air Force MTF with urology services.

# Information required for <u>waiver renewal</u>:

- A. Brief summary of previous stone history, work-up and prevention steps.
- B. If there is an interval history of additional kidney stone(s), detailed account of episode(s), treatment and prevention steps taken (Urology consult included).
- C. Radiological evidence demonstrating no new stones and no growth or movement of retained stones. A KUB is recommended for routine follow-up in the absence of symptoms during the waiver period. A CT may be necessary if the patient has a history of radiolucent stones (such as uric acid stones) or if the patient has experienced symptoms.
- D. If on prevention medication or initial 24-hour urine stone risk analysis was abnormal, then annual 24-hour urine to monitor impact of intervention.

#### III. Overview.

Urinary stone disease is the third most frequent urinary tract disorder, exceeded in frequency only by infections and prostatic disease. Men are affected more frequently than women, with a ratio of 2:1. Incident rates are highest in non-Hispanic Caucasians, followed by Hispanics, then African-Americans and other racial/ethnic groups. Initial presentation most commonly occurs in the third and fourth decades. The incidence of urolithiasis is increasing for both men and women, such that 13% of men and 7% of women will be diagnosed with a kidney stone during their lifetime. Diet and fluid intake are important factors in the development of urinary stones. Persons with diets high in protein and/or sodium may have higher rates of stone disease, and persons in sedentary occupations have a higher incidence of stones than manual laborers. Genetic factors also contribute to urinary stone formation, such as for patients with cystinuria and renal tubular acidosis.

The disease's clinical course is usually that of a gradual onset of flank, abdominal or back pain over an hour or more before acute colic pain onset. Pain (renal colic) usually is described as sharp, severe and localized to the flank and may be associated with nausea and/or vomiting. It may occur episodically and radiate anteriorly over the abdomen or be referred to the ipsilateral testis or labium. If the stone becomes lodged at the ureterovesical junction the patient may complain of marked urinary urgency and frequency. Stone size does not correlate well with severity of symptoms. Urinalysis usually reveals microscopic or gross hematuria.

# **EVALUATION OF NEPHROLITHIASIS**

In initial evaluation, the first radiograph usually obtained is the plain kidney-ureter-bladder (KUB) film. Unenhanced helical computed tomography (CT) is the most sensitive imaging method to confirm (99% diagnostic accuracy) the diagnosis of a urinary stone in a patient with acute flank pain; it also helps with the measurement of stone density and may guide treatment—stones with density > 1000 Hounsfield units do not respond as well to lithotripsy. Due to potential hazards of increased radiation exposure, CT scans should be used sparingly and judiciously. If a KUB is sufficient for performing follow-up, then it should be used instead of CT. Intravenous pyelogram (IVP) is used very infrequently now but can also be helpful in diagnosis and treatment planning. Ultrasound is a noninvasive method for demonstrating both the urinary stone and the resultant hydronephrosis and has a high specificity, but low sensitivity.<sup>4</sup>

Urinary calculi are polycrystalline aggregates composed of varying amounts of crystalloid and a small amount of organic matrix. There are five major types of urinary stones: calcium oxalate, calcium phosphate, struvite, uric acid, and cystine. The following requirements are needed for urinary stone formation: (1) formation of a crystal nidus through nucleation, (2) retention of the nidus within the urinary tract, and (3) growth of the nidus to a size sufficient to cause symptoms or be visible on imaging. For crystals to occur, the urine needs to be supersaturated with the salt in question. Intermittent supersaturation, as seen during periods of dehydration or after meals, is sufficient. As a group, stone formers excrete larger crystals and crystal aggregates than non-stone formers and have lower levels of stone inhibitors.<sup>5</sup>

Approximately 75% of renal stones are composed of calcium oxalate. Furthermore, approximately 50-75% of patients with calcium oxalate stones have hypercalciuria, the most common urinary abnormality predisposing to this type of stone disease. Etiologies of hypercalciuria include metabolic acidosis (RTA), hyperthyroidism, malignancies with bone metastases, corticosteroid treatment, vitamin D excess (exogenous or diseases such as sarcoidosis), and hyperparathyroidism. Approximately 5% of individuals with hypercalciuria have primary hyperparathyroidism. A significant number of hypercalciuric patients are classified with "idiopathic hypercalciuria," which is a diagnosis of exclusion made when the particular etiology of the hypercalciuria cannot be identified. Hypercalciuria is diagnosed with the help of a 24-hour urinary calcium excretion; the upper limit of normal is 4 mg (0.1 mmol)/kg body weight.

Hyperoxaluria may predispose to the formation of calcium oxalate stones and hyperuricosuria may predispose to the formation of uric acid stones, calcium stones, or a combination of both. Hyperoxaluria will result in an elevated urinary oxalate level. Normal level for both males and females is about 45 mg/day. If due to dietary excess (spinach, rhubarb, Swiss chard, cocoa, beets, peppers, wheat germ, pecans, peanuts, okra, chocolate and lime peel) the maximum would be 50-60 mg/day. A level above 60 mg/day should be considered abnormal. Hyperuricosuria will display an elevated urinary uric acid level. Levels greater than 800 mg (4.8 mmol)/day in men and 750 mg (4.5 mmol) in women may predispose to calcium oxalate stone formation via heterogeneous nucleation or reduction of naturally occurring urinary inhibitors.

Struvite stones, also called infection stones, represent 10-20% of renal stones. They consist of magnesium, ammonium and phosphate, mixed with carbonate. Two conditions must exist for the crystallization of struvite: urine pH of  $\geq$ 7.2 and ammonia in the urine. This is caused by urea-

splitting bacteria with the generation of ammonia. The usual causative bacteria include Proteus, Klebsiella, Pseudomonas species and Enterococci (excluding E. coli). Those who produce only struvite stones may present with large stones that cause bleeding, obstruction, or infection without stone passage. Struvite stones require complete surgical removal and possibly long-term antibiotics.

Calcium phosphate stones represent around 5% of all stones; these can be caused by renal tubular acidosis or hyperparathyroidism. The laboratory tests for this stone type are blood pH and serum bicarbonate level. If metabolic acidosis is present, along with 24-hour urinary pH > 6.5, hypercalciuria and hypocitraturia treatment is indicated. Therapy is initiated with potassium alkali and close monitoring of urinary pH, citrate and calcium. Uric acid stones also account for 5% of all stones. These usually occur in the presence of low urinary pH (5.1-5.9) and urinary uric acid levels  $\geq 1200$  mg (7.1 mmol) excreted daily. Treatment is accomplished by raising the urinary pH to 6.0-6.5 with potassium citrate and treating with allopurinol.

Cystine stones represent less than 1% of all stones. This etiology is secondary to a hereditary defect of amino acid transport. Cystine stones are often multiple, large and may form staghorns. The peak clinical expression is in the third and fourth decade. Cystine stones form because cystine is poorly soluble in the range of normal urinary pH. A level > 250 mg/24 hours is usually diagnostic of cystinuria. Hydration and alkalinization of the urine above pH of 7.5 is considered first-line treatment.<sup>7</sup> If volume plus pH adjustment are insufficient, treatment with penicillamine or tiopronin is utilized (these are not aeromedically acceptable medications).

Observational studies describe the natural history of asymptomatic renal calculi. The risks for development of pain or need for intervention depend in part on stone size and location, with larger stones more likely to require intervention. In a 2004 review of 300 patients, the risk for progression of stones was followed for a mean of 3.26 years. In this report, 77% experienced disease progression, which was defined as the need for surgical intervention, development of pain, or stone growth on serial imaging. These investigators identified that renal pelvic stones (which are free-floating) incurred the greatest risk of surgical intervention. An earlier report describes a similar rate of symptomatic events, with 32% of 107 patients with asymptomatic stones developing symptoms over a mean follow up of 31.6 months and 17% requiring surgical intervention. A 2010 study demonstrated that approximately 1 in 5 adults with asymptomatic urolithiasis will experience symptoms during a 10-year period. This equates to an approximate 2% risk/year of symptomatic stone disease.

While some have advocated observation for lower pole calculi based on the theory that gravity will prevent them from migrating, the above 2004 study did not find a significant difference in need for intervention based on stone location in upper, interpolar or lower pole calyces. A newer study in 2007 described 24 patients with asymptomatic lower pole stones who were followed for an average of 53 months and found that 33% experienced stone growth and 11% required intervention due to pain, obstruction or persistent gross hematuria. The rate of stone growth correlated positively with initial size of stone. <sup>11</sup>

Many have raised the question of whether there is a stone size threshold below which the risk for symptoms and progression is negligible, or at least less than the risks of a stone treatment intervention. This issue has been investigated through observational studies of residual fragments

after various stone procedures, including extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PN) and ureteroscopy. Some have designated small residual calculi with the term "clinically insignificant residual fragments" (CIRF), and various authors have attempted to identify a size below which intervention should be discouraged. The size threshold for CIRFs has been reported variously, from less than 2 mm to 4 mm. There is a tendency to observe these small fragments for a number of reasons. Many settle in lower pole calyces and are held stationary by gravity. It can be difficult to eradicate smaller stones, especially when they are 2 mm or less, because they are harder to localize on fluoroscopy and harder to engage with ureteroscopic baskets. The majority of stones 4 mm or less will pass spontaneously, so the cost and risk of surgical intervention are felt to exceed the benefits of treating these smaller stones for many patients.

Stone clearance and stone-free rates after ESWL vary considerably, ranging from 30-60% (depending on the ESWL machine and imaging used to detect fragments), and it is likely that residual retained fragments contribute to a persistent risk for growing stones in those treated with ESWL alone. Much higher stone-free rates can be achieved with physical extraction of stones via ureteroscopy or PN, but to date there has not been a randomized prospective trial investigating ureteroscopy vs. observation for asymptomatic renal stones.<sup>12</sup>

There have been several studies in the past decade looking at the natural history of residual fragments after ESWL. Most have shown that a significant number of such patients develop stone growth and a symptomatic episode requiring intervention. Any urologists continue to advocate observation with close follow-up for patients with residual stones  $\leq 4$  mm after an intervention due to the high rate of spontaneous passage of such stones. Despite consequential rates of stone growth, development of symptoms, and need for intervention, this is a safe and cost-effective management plan when patients have ready access to emergency medical and urology care. It is important to note that, while these smaller stones frequently pass spontaneously, they do not pass painlessly.

## TREATMENT OF NEPHROLITHIASIS

In most cases, stones < 5 mm in diameter will pass spontaneously but will take variable time to do so depending on their location at presentation. Hydration is helpful to facilitate passage of small stones.

<u>Ureteral stones</u>: Prediction of spontaneous stone passage is difficult. Stones less than 5 mm in diameter often pass spontaneously, especially in the distal ureter. In such cases, conservative observation with pain medication is appropriate for the first four weeks, as long as no infection is present. In a 1999 study of 75 subjects, 95% of stones < 4 mm passed spontaneously within 40 days, and 50% of subjects with stones  $\geq$  5 mm required intervention for refractory symptoms or failure of the stone to pass. Spontaneous passage of ureteral stones can be facilitated with hydration and oral alpha-1 adrenergic antagonists.  $^{19-21}$ 

Individuals with large stones (not likely to pass), evidence of infection, refractory symptoms or high-grade obstruction should be considered for intervention. Persistent ureteral obstruction for  $\geq 4$  weeks can increase the likelihood of renal damage in previously normal kidneys. If spontaneous stone passage has failed, therapeutic intervention is required. Ureteroscopic stone extraction or

ESWL is used to extract or fragment stones from the proximal, mid or distal ureter. Complications during ureteroscopic extraction increase as the duration of conservative observation increases beyond six weeks. It should be noted that ESWL is not without its own complications. Patients that are at increased risk of bleeding (e.g. coagulopathy) or are obese may have poorer outcomes with ESWL, and these are two considerations that could influence the choice of initial intervention, in addition to other factors such as stone location and size. Percutaneous removal can be used for ureteral stones but is generally reserved for those too large to be treated effectively for ureteroscopy or when the ureter cannot be accessed from the lower urinary tract. Open surgery and blind basket extraction have fallen out of favor as ureteral and nephroscopes have improved in capability. Indications for earlier intervention include intractable pain, fever, or persistent nausea and vomiting.

Renal stones: Retained stones in the renal parenchyma, renal cyst, or calyceal diverticulum rarely migrate into the collecting system and therefore should be followed with serial abdominal radiographs and/or ultrasound. If calculi are growing or becoming symptomatic, intervention should be considered. Direct visualization with ureteroscopy may be required to determine if stones are free-floating in the collecting system or retained in parenchyma or other enclosed spaces. Renal stones in a papillary duct or more distal part of the collecting system, such as Randall's plaques are more likely to enter the collecting system. However, removal of these calculi may not be possible if they cannot be visualized. Renal stones < 2 cm in diameter can be treated successfully with ureteroscopy, ESWL, or Percutaneous Nephrolithotomy (PN). Larger stones and those located in lower pole calyces may not respond well to ESWL but can be successfully treated with ureteroscopy or PN, depending on patient anatomy and other clinical considerations.

Prevention of recurrence: Those afflicted with stone disease are encouraged to remain well-hydrated (>2L/day) and maintain a diet restricted in sodium and animal protein intake.<sup>24</sup> Excess intake of oxalates and purines can increase the incidence of stones in predisposed individuals. Medical therapy is dictated by a metabolic evaluation that includes 24-hour urine collection for a variety of stone-forming metabolites, as well as an assessment of parathyroid function and calcium metabolism. Medical therapy is effective in reducing the risk for future nephrolithiasis, and can also reduce the growth and risk of existing stones becoming symptomatic.<sup>25, 26</sup> Treatment may include a thiazide diuretic for hypercalciuria, allopurinol or potassium citrate for hyperuricosuria and potassium citrate for hypocitraturia, depending on factors identified by a metabolic evaluation. In the absence of a defined metabolic abnormality, empiric therapy with potassium citrate has also been shown to reduce the risk of future symptomatic episodes.<sup>27</sup>

## IV. Aeromedical Concerns.

The pain of renal colic can be severe and is potentially incapacitating in flight. A few cases of some degree of in-flight incapacitation have been reported. Missions have been curtailed due to renal colic in aircrew. The aviation environment can be conducive to renal calculi formation; conditions of dehydration, extremes of temperature, sedentary work and adverse dietary factors are commonly experienced by aircrew members. Each case must be determined individually after consultation with urology and radiology. <sup>29</sup>

| ICD-9 codes for renal stones      |             |
|-----------------------------------|-------------|
| 592 Calculus of kidney and ureter |             |
| 788.0                             | Renal colic |

| ICD-10 codes for renal stones |                               |
|-------------------------------|-------------------------------|
| N20.0                         | Calculus of kidney            |
| N20.1                         | Calculus of ureter            |
| N20.9                         | Urinary calculus, unspecified |
| N23                           | Unspecified renal colic       |

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#### WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of Jun 2012

By: Dr Dan Van Syoc

Reviewed by Col Brandon Horne, AF/SG consultant for orthopedic surgery, and AFMSA staff

## **CONDITION:**

Retained Orthopedic Hardware and Joint Replacement (Jan 2018)

## I. Waiver Consideration.

Individuals with fractures are grounded until evidence of bone healing and return of full function can be documented. For fractures with retained hardware, waiver is required for FC I/IA, II, III, and SWA personnel when there is obstruction of motion or if easily irritated/painful when hit/pressure applied (MSD K82). MEB and waiver for all flying duties is required for all joint replacements and prosthetics if it results in ongoing duty or deployment limitations for over a year, or requires ongoing specialist f/u more than annually, or causes frequent absences from duty (MSD K65), and applies to ATC/GBO, SWA and Operational Support Flying personnel. For joint prosthetics an unrestricted FC II and III waiver may be considered. Joint prosthetics are not considered waiverable for FC I/IA, untrained FC II and FC III, and for parachute duties (SWA). Joint replacements without complication are disqualifying for flying duties and require waiver (MSD K70) only for FC I/IA, II, III, and SWA personnel.

Table 1: Summary of Clinical Conditions and Waiver Potential

|                  | Flying Class   Condition   Waiver Potential |                     |  |
|------------------|---|---------------------|--|
| Flying Class     | Condition                                   |                     |  |
|                  |   | Waiver Authority    |  |
| I/IA             | Retained orthopedic device with no          | No waiver required, |  |
| Untrained        | pain or limitation of motion (able to       | medically qualified |  |
| II/III/SWA       | lead physically active lifestyle)           |                     |  |
|                  |   |                     |  |
|                  | Retained orthopedic device with             | Maybe               |  |
|                  | obstruction of motion or if easily          | AETC                |  |
|                  | irritated/painful when hit/pressure         |                     |  |
|                  | applied                                     |                     |  |
|                  | аррпец                                      |                     |  |
|                  | Joint replacement                           | No                  |  |
|                  | Joint replacement                           | AETC                |  |
| II/III/SWA       | Detained authomodic devices with me         | _                   |  |
|                  | Retained orthopedic device with no          | No waiver required, |  |
| ATC/GBO          | pain or limitation of motion (able to       | medically qualified |  |
|                  | lead physically active lifestyle)           |                     |  |
|                  |   |                     |  |
|                  | Retained orthopedic device with             | Maybe               |  |
|                  | obstruction of motion or if easily          | MAJCOM              |  |
|                  | irritated/painful when hit/pressure         |                     |  |
|                  | applied                                     |                     |  |
|                  |   |                     |  |
|                  | Joint replacement, minimum four             | Yes†                |  |
|                  | months post-op.+                            | MAJCOM              |  |
| Individuals with | Retained orthopedic device with no          | No waiver required, |  |
| parachuting      | pain or limitation of motion (able to       | medically qualified |  |
| duties (not      | lead physically active lifestyle)           | ,                   |  |
| including        | prijotemij active intestyte)                |                     |  |
| emergency        | Retained orthopedic device with             | Maybe               |  |
| bailout)         | obstruction of motion or if easily          | MAJCOM              |  |
| vanout)          | •   | IVIAJCOIVI          |  |
|                  | irritated/painful when hit/pressure         |                     |  |
|                  | applied                                     |                     |  |
|                  |   |                     |  |
|                  | Joint replacement                           | No                  |  |
|                  |   | MAJCOM              |  |

<sup>†</sup> If dislocation has occurred ACS review of case is required. If THA dislocation occurred within first 6 weeks then waiver more likely and will require minimum 6 months post dislocation.

Review of AIMWTS through Jun 2017 showed 49 aviators with an AMS containing the diagnosis of <u>hip replacement</u> with 3 disqualifications (1 FC II and 2 FC III). Breakdown of the cases was as follows: 34 FC II cases, 12 FC III cases and 3 ATC/GBC cases. Two cases were disqualified case was due to another medical condition and the third case was disqualified secondary to pain after surgery. The majority had hip replacements due to severe osteoarthritis.

<sup>+</sup> This includes "minimally invasive" hip replacement procedures.

Review of AIMWTS through Jun 2017 showed 26 cases of <u>knee replacement</u> with 4 disqualifications (2 FC II and 2 FC III). There were 14 FC II cases and 12 FC III cases. One of the disqualified cases was due to CAD, two for multiple medical issues, and the fourth for severe neck pain.

Review of AIMWTS through Jun 2017 showed 135 cases of <u>retained orthopedic hardware</u> with a total of 13 disqualifications (2 FC II and 11 FC III). Breakdown of the cases was as follows: 8 FC I/IA, 49 FC II, 75 FC III, and 1 ATC case. Of the 13 DQ cases, 8 were initial certifications and were related to the hardware and the other 5 were for other medical conditions.

# II. Information Required for Waiver Submission.

The aeromedical summary should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

If the patient requires an <u>initial waiver</u> for retained orthopedic hardware, the AMS should include the following:

- A. History brief summary of trauma, surgery and recovery, complications, symptoms, current activity level, and medications.
- B. Physical addressing range of motion, muscle strength, point tenderness.
- C. Operative reports.
- D. X-ray documenting radiographic healing.
- E. Orthopedic consult that addresses hardware, muscle strength, range of motion of proximal and distal joint, limitations in activities.
- F. If functionality is reduced, include a statement of demonstrated ability (SODA) performing tasks in aircraft.

The AMS for waiver renewal for retained orthopedic hardware should include the following:

- A. History brief summary of trauma, surgery and recovery, complications, symptoms, current activity level, and medications.
- B. Physical addressing range of motion, muscle strength, point tenderness.
- C. Orthopedic consult, if symptoms changed.

The AMS for initial waiver for prosthetic joint should include the following:

- A. History of symptoms, limitations prior to surgery, summary of surgery and recovery, present level of activity, medications, and limitations.
- B. Physical addressing range of motion, muscle strength.
- C. Orthopedic consult range of motion, muscle strength, activity level, limitations.
- D. Operative reports.
- E. X-rays documenting radiographic healing.
- F. Include a statement of demonstrated ability (SODA) performing tasks in aircraft.
- G. Medical evaluation board (MEB) results.

The AMS for waiver renewal for prosthetic joint should include the following:

A. History and physical – to include summary of surgery and recovery, present level of activity, medications, and limitations.

B. Orthopedic consult

C. X-rays results.

#### III. Overview.

Fractures requiring open reduction and internal fixation (ORIF) are fairly common among our active aircrew member population. Less common are degenerative joint diseases requiring prosthetic joint implants due to the relatively young population served. This waiver guide will discuss retained orthopedic hardware and total hip and knee replacements. Fixation devices in the spine and artificial intervertebral disks are considered separately in the "Herniated Nucleus Pulposus (HNP) and Spinal Fusion" waiver guide.

## RETAINED ORTHOPEDIC HARDWARE:

Retained hardware devices, except in the case of joint replacement, consist primarily of screws, plates, wires and intramedullary rods (nails). These components are placed to stabilize the fracture and allow for adequate healing. Fracture healing time depends on the nature of the fracture (amount of energy involved in creating the fracture, disruption of soft tissue around the fracture, and the particular bone involved). In the vast majority of fractures, medical standard of care no longer dictates removal of fixation devices. In some cases after adequate bone regeneration, implant removal may be indicated because of patient preference or to restore skeletal strength (usually in children). Additional removal may be required if the device causes pain (loose screw) or reduction in function.

For fractures with retained hardware, waiver is required when there is obstruction/limitation of motion or if the hardware is easily irritated/painful when hit or when pressure is applied in common activities. Usually, to rectify these symptoms the hardware is removed, correcting the problem. Waiver is required in those cases when the device can't be removed or the individual declines removal.

# **JOINT REPLACEMENT:**

Over 600,000 total knee arthroplasties (TKAs) are done in the US every year. The knee joint is made up of three compartments; the lateral, medial and patellofemoral. Damage to the cartilage from osteoarthritis, inflammatory arthritis, avascular necrosis, tumors or congenital deformities are the causes for the need for TKA, with the majority due to osteoarthritis and rheumatoid arthritis. TKAs are indicated in individuals who have failed conservative [activity modification, weight reduction, physical therapy, shoe insoles, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, glucosamine and chondroitin sulfate, and/or use of assistive device (cane)] or previous surgical treatment [osteotomy, lavage and surgical debridement, cartilage preserving or restoring] for a deteriorated knee joint and continue to have persistent, debilitating pain and significant curtailment in activities of daily living. Unicompartmental knee replacement as treatment in unicompartmental, noninflammatory situations has been used as an alternative to TKA or osteotomy. TKA consist of a femoral, tibial and patella component. Designs can be either

posterior cruciate ligament sparing or not; various metal and polyethylene component combinations. Fixation techniques include cemented (both femoral and tibia), cementless or hybrid (usually femoral cemented and tibia not). The cement serves as grout between the implant and bone. Cementless technique relies on bony ingrowth into or onto porous implant surface. There is a wide choice of implants and large variation between surgeons and nations. Approximately 90 to 95% of TKAs survive to the 10-year point.<sup>2</sup> Complications include thromboembolism, infection, patellofemoral disorders, prosthetic fractures, peroneal nerve palsy, polyethylene wear, and aseptic failure. Risk of intraoperative infection is less than 2% after knee replacement.<sup>3</sup> A recent study of outcome in active duty Army members following TKA showed that 82% had resumed their military career.<sup>4</sup>

Over 150,000 total hip arthroplasties (THAs) are performed in the US every year. The main reason for THA is osteoarthritis of the hip; less common is for advanced rheumatoid arthritis or avascular necrosis. Over 90% of THA are working successfully, pain-free and without complication 10 to 15 years postoperatively.<sup>5</sup> THAs are indicated in individuals who have failed conservative [weight reduction, physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, glucosamine and chondroitin sulfate, and/or use of assistive device (cane)] or previous surgical treatment [core decompression, intertrochanteric osteotomy, periacetabular osteotomy, surgical dislocation and debridement, resection arthroplasty, hip arthroscopy] for a deteriorated hip joint and continue to have persistent, debilitating pain and significant curtailment in activities of daily living. All THAs consist of three parts; femoral component, acetabular component and a bearing surface. Fixation of the components to the bone is either with cement or cementless. Cementless acetabulum is the most common implant and for the femoral implant cementless is used most often in younger individuals with good bone stock. For years the standard bearing surface has been a metallic femoral head which articulates with a polyethylene acetabular liner. Other bearing surfaces developed and used include ceramic on polyethylene, ceramic on ceramic and metal on metal. "Minimally invasive" replacement procedures, such as hip resurfacing where the femoral neck is preserved thus usually requiring more acetabular side bone removal or procedures that decrease the incision size to less than 10 cm (up to 15 cm) still have extensive soft tissue trauma and require experienced orthopedic surgeons. It should be noted also that recovery times for these procedures are not necessarily shorter.

Complications of THA include heterotopic ossification, dislocation, nerve damage, fracture, infection, loosening, leg length discrepancy and thromboembolism. Dislocation remains a common and problematic complication after primary THA with rates of approximately 2% to 5%. Once dislocation has occurred, the risk of redislocation is high; incidence of 33%. Most dislocations occur within the first three months after surgery. Proximal femoral fracture is a relatively common intraoperative occurrence during total hip arthroplasty (THA) with a reported incidence of 2-6%. In one study the risk factors for fractures include anterolateral approach, uncemented femoral fixation and female sex. Risk of intraoperative infection is less than 1% after hip replacement. In one study of 63 consecutive episodes of infection associated with hip prostheses during a 16-year-period, 29% of cases were early (less than 3 months after surgery) infections, 41% were delayed (3 to 24 months after surgery) and 30% were late (more than 24 months after surgery) infections. The risk for fracture-fixation device infections is approximately 2%. Femoral and acetabular loosening is the most common long-term complication and most common indication for revision.

Guidelines for acceptable activity after hip and knee replacement are not well defined. The following is from a 2002 article summarizing the literature on exercise recommendations after total joint replacement and suggested a scientifically based guideline. <sup>12</sup> Physical activity is important for general health and also increases bone health which improves prosthesis fixation and decreases early loosening. Factors such as wear, joint load, intensity and the type of prosthesis must be taken into account when recommending activity after TKA and THA. There is evidence that the reduction in wear is one of the main factors in improving long-term results after total joint replacement. Wear is dependent on load, number of steps and material properties of the prosthesis. The most important question is, whether a specific activity is performed for exercise to obtain and maintain physical fitness or whether an activity is recreational only. To maintain physical fitness an endurance activity will be performed several times per week with high intensity. Since load will influence the amount of wear exponentially, only activities with low joint loads such as swimming, cycling or possibly power walking should be recommended. If an activity is carried out on a low intensity and therefore recreational base, activities with higher joint loads such as skiing or hiking can also be performed. It is unwise to start technically demanding activities after total joint replacement, as the joint loads and the risk for injuries are generally higher for these activities in unskilled individuals.

It is important to distinguish between suitable physical activities after TKA and THA. For TKA it is important to consider both the load and the knee flexion angle of the peak load, while for THA the flexion angle does not play an important role. During activities such as hiking or jogging, high joint loads occur between 40 to 60 degrees of knee flexion where many knee designs are not conforming and high polyethylene inlay stress will occur. Regular jogging or hiking produces high inlay stress with the danger of delamination and polyethylene destruction for most current total knee prostheses. Based on these design differences between hip and knee replacements it is prudent to be more conservative after TKA than after THA for activities that exhibit high joint loads in knee flexion. For THA, obesity and advancing age negatively impact walking activity after THA. A recent study looking at gender differences with TKA revealed that men have higher levels of function and activity both prior to and after TKA than women. It is unsure how this translates to our aviator population.

## IV. Aeromedical Concerns.

The chief aeromedical concern of aircrew members with retained hardware is that the underlying orthopedic diagnoses (e.g. fracture, ligament damage) have healed. Once healed, other concerns are discomfort due to the hardware, adequacy of function, soft tissue inflammation, and increased risk of infection leading to osteomyelitis, all of which could lead to flight safety issues and compromise mission completion. Aeromedical concerns for THA and TKA include dislocation, fracture, leg length discrepancy and thromboembolism. History of dislocation of THA suggests that the individual's hip is unstable and will continue to be unstable or the individual is non-compliant with hip precautions; neither situation is conducive to flight safety or mission accomplishment. Parachute duty places a repeated trauma to a TKA and THA, with the risk of catastrophic failure. Ejection would be a one-time occurrence in an "emergency situation only." Finally, current generation joint prostheses have an expected life span of 10 to 20 years.

| ICD-9 codes for Joint Replacement |   |
|-----------------------------------|---|
| 81.5                              | Joint replacement for lower extremity       |
| 81.51                             | Total hip replacement                       |
| 81.52                             | Partial hip replacement                     |
| 81.53                             | Revision of hip replacement, not otherwise  |
|                                   | specified                                   |
| V43.64                            | Hip joint replacement                       |
| V43.60                            | Unspecified joint replacement               |
| 81.54                             | Total knee replacement                      |
| 81.55                             | Revision of knee replacement, not otherwise |
|                                   | specified                                   |
| V43.65                            | Knee joint replacement                      |

| ICD-9 codes for Retained Orthopedic Hardware |                                      |  |
|--|--------------------------------------|--|
| 79.8   | Open reduction of dislocation        |  |
| 79.9   | Unspecified operation of bone injury |  |
| V54.01                                       | Hardware removal                     |  |
| 996.49                                       | Internal implant orthopedic device   |  |

| ICD-10 codes for Joint Replacement |                               |
|------------------------------------|-------------------------------|
| 0SR9                               | Hip joint, right              |
| 0SRA                               | Hip joint, acetabular surface |
| 0SRB                               | Hip join left                 |
| 0SRC                               | Knee joint, right             |
| 0SRD                               | Knee joint, left              |

| ICD-10 codes for Retained Orthopedic Hardware           |   |  |
|---|---|--|
| Z96.9   | Presence of functional implant, unspecified |  |
| Z47.2 Encounter for removal of internal fixation device |   |  |

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- 14. Cherian JJ, O'Connor MI, Robinson K, et al. A Prospective, Longitudinal Study of Outcomes Following Total Knee Arthroplasty Stratified by Gender. J Arthroplasty, 2015; 30: 1372-77.

## Retinal Holes, Retinal Tears, Retinal Detachment, and Retinoschisis (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons, (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col Ian D. Gregory (AFMRA Physical Standards Development Chief)

# **Significant Changes:**

New Ground Based Operator (GBO) Standards. MSD C39-42.

## I. Waiver Consideration

Bilateral retinal detachment is disqualifying for all classes and for retention. Unilateral retinal detachment from organic progressive disease or with persistent defects may be disqualifying for all classes and for retention. Retinal breaks and retinoschisis are only disqualifying for Flying Classes I/IA, II, III, and SWA. Low risk atrophic retinal holes with a refraction less than or equal to -5.50 are not considered disqualfying. Waiver potential exists for low risk atrophic retinal holes with refraction from -5.75 to -8.00 diopters.

Table 1: Waiver potential for Retinal Holes, Retinal Tears, Retinal Detachment, and Retinoschisis.

| Flying Class (FC) | Waiver Potential   | Waiver Authority | ACS Review or Evaluation |
|-------------------|--------------------|------------------|--------------------------|
| I/IA              | Maybe <sup>1</sup> | AETC             | Yes                      |
| II/III            | Yes <sup>2</sup>   | MAJCOM           | Yes                      |
| ATC/GBO/SWA/OSF   | Yes <sup>3,4</sup> | MAJCOM           | Yes                      |

<sup>1</sup> Low risk features for retinal detachment are defined as absence of symptoms (flashes or floaters), no prior history of retinal detachment, no subretinal fluid, myopia between -5.75 to -8.00 diopters, and no evidence of vitreo-retinal traction. In addition, there should be no retinal breaks at the edge or outside the area of lattice degeneration, except in the case of operculated peripheral retinal hole.

- 2. Untrained FC II/III treated similar to FC I/IA.
- 3. Not disqualifying if treated and/or determined to be stable by a vitreo-retina specialist.
- 4. No waiver potential if bilateral retinal detachment or unilateral retinal detachment resulting from organic progressive disease, and/or associated with diplopia, field of view <20 degrees, or loss of acuity below standards.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations; MEB may be required for retinal detachment. If the treating ophthalmologist or retinal specialist determines surgical treatment is required then waiver submission should occur after adequate recovery time without complications and adequate pigment changes in the post-laser scar has occurred (one month minimum). If no treatment is required, then the 1 month waiting period prior to waiver submission is not required. All initial waivers (or recurrence of retinal tear or detachment) require an ACS evaluation/review.

### A. Initial Waiver Request:

- 1. List and fully discuss all clinical diagnoses requiring a waiver.
- 2. Complete aeromedical history to include pertinent negatives (trauma, myopia, lattice degeneration, etc.), high-risk features, or treatment(s), if applicable.
- 3. Optometric exam to include:
  - a. Manifest refraction (previous refraction if underwent CRS)
  - b. Visual acuity
  - c. Humphrey 30-2 visual field
  - d. Amsler grid
  - e. CCT results from each eye individually (if macular involvement)
- 4. Ophthalmology or retinal specialist consultation to include: history, positive risk factors, exam findings, treatment(s), and surgical outcome.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

### B. Renewal Waiver Request:

- 1 Interval history to include presence or absence of current visual symptoms and operational impact of condition.
- 2 Results of interval ophthalmology exams.
- 3 Summary of any interval medical or surgical treatments (if required).
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

# **III. Aeromedical Concerns**

Retinal holes and tears can lead to retinal detachment. Retinal detachment can result in loss of visual acuity, loss of stereopsis, visual distortion, visual field loss, relative night blindness, reduced color vision, and lowered contrast sensitivity. The specific visual impact depends on the area and extent of the retina involved and the success of any reattachment surgery. In 90% of cases, eyes with no macular detachment present can be expected to have 20/40 vision or better following surgery. Consideration must also be given to the risk of progression, recurrence or involvement of the fellow eye based on the mechanism of retinal pathology, or type of retinal detachment. Although routine exposure to G-forces has not been shown to increase the risk of retinal detachment, the risk is increased with pre-existing vitreoretinal abnormalities, especially in the case of tractional retinal detachment, and this should be considered in the case of unrestricted waivers. All patients with documented retinal holes or breaks should have their manifest refractions included in the Aeromedical Consultation Service (ACS) referrals (these should be pre-corneal refractive surgery measurements if applicable), as higher levels of myopia lend to a higher risk of retinal detachment as discussed above. This risk is due to the fact that myopic eyes tend to have longer axial lengths, which is the real risk factor for retinal detachment. The ACS Ophthalmology Branch is currently investigating this association and its applicability to aeromedical standards. All retinal breaks need careful examination to identify the types of holes present and to determine if active vitreo-retinal traction or other signs of impending retinal detachment are present. This can be accomplished by any ophthalmologist or vitreo-retinal subspecialist (retinal detachment) but should also be reviewed by the ACS once the underlying disease process has stabilized.

AIMWTS search in Sep 2019 back to 1 Jan 2014 revealed 241 members with an AMS containing one of the above retinal diagnoses. There were 21 cases that were disqualified. Breakdown of the cases revealed: 23 FC I/IA cases (3 disqualified), 106 FC II cases (3 disqualified), 7 RPA pilot cases (2 disqualified), 92 FC III cases (11 disqualified), 4 ATC/GBC cases (0 disqualified), 6 SWA cases (1 disqualified), and 3 MOD cases (1 disqualified).

| ICD-9 codes for retinal hole, retinal detachment, and retinoschisis |                    |  |
|---|--------------------|--|
| 361.3   | Retinal holes      |  |
| 361.31  |                    |  |
| 361.0   | Retinal detachment |  |
| 361.2   |                    |  |
| 361.8   |                    |  |
| 361.9   |                    |  |
| 361.1   | Retinoschisis      |  |

| ICD-10 codes for retinal hole, retinal detachment, and retinoschisis |  |  |
|--|--|--|
| H33.309  | Unspecified retinal break, unspecified eye |  |
| H33.329  | Round hole, unspecified eye                |  |
| H33.2  | Serous retinal detachment                  |  |
| 0, 1, 2, 3   |  |  |
| H33.8  | Other retinal detachments                  |  |
| H33.10   | Unspecified retinoschisis                  |  |
| 0, 1, 2, 3   |  |  |

# **IV. Suggested Readings**

1. Greven CM. Retinal Breaks. Ch. 6.37 in Yanoff: Ophthalmology, 4th ed., Saunders, 2013.

### Rheumatoid Arthritis (Dec 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

Significant Changes: Content updated to reflect national guidelines.

#### I. Waiver Consideration

Rheumatoid arthritis is disqualifying for all flying duties, GBO duties, ATC duties, and special warfare duties. It is also disqualifying for retention. Aeromedical waiver is usually not recommended for untrained personnel. Factors considered when assessing suitability for aeromedical waiver include the severity of disease at diagnosis, evidence of clinical remission, whether treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the risk associated with specific medication(s), the individual service member's tolerance of the medication(s) and adherence to therapy, and the cumulative risk of all associated complications and/or extra-articular manifestations. Waiver can be considered once an individual is in disease remission on a stable, aeromedically-approved medication regimen, without adverse effects. Use of any medication not included on a career-field approved medication list is independently disqualifying and will be considered on a case-by-case basis.

Cervical spine involvement is common in individuals with rheumatoid arthritis, predisposing individuals to atlantoaxial instability and/or atlantoaxial subluxation. Thus, pilots eligible for waiver will be restricted to a FC IIB waiver, non-ejection seat aircraft. Additionally, special warfare personnel with cervical spine involvement demonstrated on imaging will be restricted from jump status. The most common imaging modality used to assess for cervical instability is plain film radiographs of the cervical spine in the following positions anteroposterior, lateral, open-mouth, flexion, and extension.

**Table 1: Waiver potential for Rheumatoid Arthritis** 

| Flying Class (FC)      | Waiver Potential <sup>1</sup> | Waiver Authority        | ACS Review or<br>Evaluation |
|------------------------|-------------------------------|-------------------------|-----------------------------|
| I/IA                   | No                            | AETC                    | No                          |
| II/III/Special Warfare | Yes <sup>2,3,4</sup>          | MAJCOM <sup>2,3,4</sup> | Yes                         |
| ATC/GBO                | Yes <sup>3,4</sup>            | MAJCOM <sup>3,4</sup>   | No                          |

- 1 Untrained personnel of any class are unlikely to receive an aeromedical waiver.
- Waiver for pilots will be restricted to FC IIB. Special warfare personnel with documented cervical involvement will be restricted from jump duties. AFMRA is the waiver authority for all restricted waivers.
- 3 Use of any medication that is not included on the approved medication list is independently disqualifying, and the MAJCOM may disqualify the service member without AFMRA or ACS review. Waiver may be considered following an ACS review on a case-by-case basis in certain low-risk individuals treated with unapproved medications. The waiver authority for all non-approved medications is AFMRA.
- 4 Individuals controlled with TNF-alpha inhibitors require AF Form 469 document the need for access to transport and refrigeration (between 36 to 46 degrees Fahrenheit) for any TDY or deployment assignment.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

### A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- 2. Consultation reports form treating rheumatologist, which should include:
  - a. Subjective symptoms and objective physical exam findings
  - b. Current treatment plan, to include tolerance and current doses of maintenance medications and all appropriate monitoring labs for those medications (e.g., biologic agents require CBC/CMP every 3-6 months and annual TB testing).
  - c. Documentation excluding/including extra-articular manifestations (i.e., ocular, pulmonary, cardiac, etc.)
- 3. All pertinent laboratory studies, including diagnostic and follow-up results.
  - a. Initial serologic testing (e.g., RF, anti-CCP, and any other serologic testing)
  - b. Updated CBC, CMP, ESR, and CRP.
- 4. Radiology reports from all diagnostic or follow-up imaging studies.
  - a. Initial and updated plain films of the hands, feet, and cervical spine in anteroposterior, lateral, open-mouth, flexion, and extension views.
- 5. Current physical examination findings with focus on musculoskeletal exam.
- 6. Dilated ocular exam if treated with hydroxychloroquine.
- 7. FL4 with RTD and ALC status.
- 8. Any other pertinent information.

9. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Current symptoms and development of any disease flares, complications, or extraarticular manifestations.
  - b. Current medications, doses, and adverse effects.
  - c. Current physical examination findings.
- 2 Consultation reports from treating rheumatologist.
- 3 Any interval imaging obtained pertaining to the rheumatoid arthritis diagnosis.
- 4 Updated CBC, CMP, ESR, and CRP.
- 5 Updated plain films of the hands, feet, and cervical spine in flexion and extension views.
- 6 Updated dilated ocular exam if treated with hydroxychloroguine.
- 7 Any other pertinent information.
- 8 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

#### III. Aeromedical Concerns

Rheumatoid arthritis (RA) is systemic inflammatory disease resulting in articular and extra-articular symptoms of aeromedical concern. The most common presentation is the development of symmetric, poly-articular synovitis of the small joints. Joint involvement with symptoms of prolonged morning stiffness, swelling, erythema, and pain potentially results in subtle performance decrement of aviation and operational duties. Untreated RA may result in damage and deformities of the joints that are irreversible. Cervical joint involvement such as atlantoaxial instability, atlantoaxial subluxation, or cranial settling, potentially results in severe neurologic sequelae or death in the event of trauma, especially if there is hyperextension or hyperflexion of the cervical spine. The most common imaging modality used to assess for cervical instability is plain film radiographs of the cervical spine in the following positions: anteroposterior, lateral, open-mouth, flexion, and extension. MRI of the cervical spine is indicated if plain film demonstrates abnormalities or individuals have radicular or myelopathic symptoms. Studies have shown a high rate of cervical involvement in individuals with rheumatoid arthritis, ranging between 43% and 86%. Individuals without any cervical involvement at the time of diagnosis have an estimated 4% to 10% annual risk of developing cervical instability. The most common symptoms of cervical involvement include neck and occipital pain. Pilots submitting a waiver for a diagnosis of rheumatoid arthritis will receive a restricted FC IIB waiver to non-ejection seat aircraft. Additionally, special warfare personnel with cervical spine involvement identified on imaging will be restricted from jump status. Rheumatoid arthritis is associated with the development of extraarticular involvement including potential ocular, pulmonary, cardiovascular, renal, neurologic, and hematologic manifestations that carry further aeromedical risk.

Many of the medications used to treat rheumatoid arthritis convey side effects incompatible with aviation or enhanced operational duties. There are multiple disease-modifying antirheumatic drugs (DMARDs) available. The first-line treatment for rheumatoid arthritis is methotrexate. Although clinically used as a first-line agent, the use of methotrexate might result in toxicity of multiple organ systems of aeromedical concern that are incompatible with flying duties. The pulmonary system is

the most concerning organ system involved in which toxicity can occur rapidly during any point of treatment, resulting in an acute pneumonitis and respiratory distress. The use of methotrexate exceeds historical waiver thresholds. The only career-field approved medications for treatment of RA are sulfasalazine, hydroxychloroquine, adalimumab, infliximab, and etanercept. Individuals treated with hydroxychloroquine require annual dilated eye exam to assess for retinal toxicity for aeromedical purposes. Biologic agents require access to transport and refrigeration (between 36 to 46 degrees Fahrenheit) for any TDY or deployment assignment.

Individuals who have received exogenous steroids for greater than a three-week duration within the last year to induce disease remission will require aeromedical assessment of the hypothalamic-pituitary-adrenal axis prior to waiver consideration (Please see the Systemic Glucocorticoid (Steroid) Treatment waiver guide).

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 18 individuals with an AMS containing the diagnosis of RA. Four individuals (22.2%) were disqualified. A breakdown of the cases was follows: 1 FC I/IA cases (1 disqualified), 9 FC II cases (2 disqualified), 0 FC III cases, 3 ATC/GBC cases (2 disqualified), 0 MOD cases, and 0 RPA Pilot cases.

| ICD-9 codes for Rheumatoid Arthritis |                      |
|--------------------------------------|----------------------|
| 714.0                                | Rheumatoid arthritis |

| ICD-10 codes for Rheumatoid Arthritis |                                   |
|---------------------------------------|-----------------------------------|
| M06.9                                 | Rheumatoid arthritis, unspecified |

## **IV. Suggested Readings**

- 1. Gillick JL, Wainwright J, and Das K. Rheumatoid Arthritis and the Cervical Spine: A Review of the Role of Surgery. *International Journal of Rheumatology*. Epub 2015; doi: 10.1155/2015/252456. https://www.ncbi.nlm.nih.gov/pubmed/26351458
- 2. Singh JA, SAAG KG, Bridges SL, and et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis and Rheumatology*. 2016; 68(1):1-25. https://www.ncbi.nlm.nih.gov/pubmed/26545940

# Salivary Gland Disorders (Apr 2019)

Reviewed: Lt Col Preston Laslie (RAM 2020), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), Lt Col Wesley Abadie (AF/SG Otolaryngology Consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

Significant Changes: New format

#### I. Waiver Consideration

Recurrent obstructive calculi of the salivary glands or ducts and salivary fistulae are disqualifying for flying classes I/IA, II, and III. Other disorders of the head and neck should prompt line-item review of the latest MSD, as several conditions are also disqualifying for ATC, GBO, and SWA duty. Malignancies of any sort are disqualifying for flying and special operational duties as well as retention. Benign tumors are considered disqualifying only if they interfere with the function or ability to wear required life support equipment or if they are likely to enlarge or be subjected to trauma during routine military service or have high malignant transformation potential. Benign tumors may require I-RILO if the condition in not remediable or ongoing specialty care is required more than annually. Chronic systemic conditions, which may involve salivary gland structures or function, are addressed under the specific condition identified (e.g., Sjögren's Syndrome, Diabetes Mellitus, and Sarcoidosis). If unfitting, I-RILO should be processed with FL-4 reflecting return-to-duty uploaded to AIMWTS prior to AMS submission. Due to the relative infrequency of salivary gland disorders in the flying population and wide variability, a case-by-case approach to waiver consideration is encouraged.

Table 1. Waiver Considerations for Salivary Gland Disorders

| Flying Class   | Disqualifying Condition   | Waiver Potential           | ACS Review/Eval          |
|----------------|---|----------------------------|--------------------------|
| (FC)           |   | Waiver Authority           |                          |
| FC I/IA        | Recurrent salivary stones   | Maybe <sup>1</sup>         | No                       |
| Initial II/III |   | AETC                       |                          |
|                |   | 35.4.1                     |                          |
|                | Salivary fistula  | Maybe <sup>1</sup>         | No                       |
|                |   | AETC                       |                          |
|                | Impaired speech or mastication or                                   | No                         | No                       |
|                | condition which precludes wear of                                   | AETC                       |                          |
|                | life support equipment  | 1210                       |                          |
|                | me support equipment  |                            |                          |
|                | Benign tumor  | Maybe <sup>1</sup>         | Yes                      |
|                |   | AETC                       |                          |
|                | Malianant tunnan  | Marila 2                   | At the discretion of the |
|                | Malignant tumor   | Maybe <sup>2</sup><br>AETC | waiver authority         |
| FC II/III      | Recurrent salivary stones   | Yes                        | No                       |
| 1 0 11/111     | Trocurrent sum vary stones  | MAJCOM                     |                          |
|                |   |                            |                          |
|                | Salivary fistula  | Yes                        | No                       |
|                |   | MAJCOM                     |                          |
|                | Impaired speech or mastication or                                   | No                         | No                       |
|                | condition which precludes wear of                                   | MAJCOM                     | 140                      |
|                | life support equipment  | WAJCOW                     |                          |
|                | me support equipment  |                            |                          |
|                | Benign tumor  | Yes <sup>1</sup>           | Yes                      |
|                |   | MAJCOM                     |                          |
|                | 3.5.41  | 3.5.4.2                    |                          |
|                | Malignant tumor   | Maybe <sup>3</sup>         | Yes                      |
| GBO/ATC        | Pagurrant calivary stones   | AFMRA<br>N/A               | N/A                      |
| SWA            | Recurrent salivary stones   | 11//1                      | 11/71                    |
|                |   |                            |                          |
|                | Salivary fistula  | N/A                        | N/A                      |
|                |   |                            |                          |
|                | Invariant annual constitution                                       | N <sub>2</sub>             | Na                       |
|                | Impaired speech or mastication or condition which precludes wear of | No<br>MAICOM               | No                       |
|                | life support equipment  | MAJCOM                     |                          |
|                | ine support equipment   |                            |                          |
|                | Benign tumor  | Yes <sup>1</sup>           | Yes                      |
|                | 6   | MAJCOM                     |                          |
|                |   |                            |                          |
|                | Malignant tumor   | Maybe <sup>3</sup>         | Yes                      |
|                |   | AFMRA                      |                          |

<sup>1.</sup> Consideration for waiver is dependent upon severity of presentation, and any associated complications and/or frequency of recurrence.

<sup>2.</sup> Waiver consideration requires at least six months has elapsed from completion of treatment (three months if excision only required) and is dependent on tumor type, staging, complications, and likelihood of recurrence.

<sup>3.</sup> May consider waiver for certain cured tumors that have a very good prognosis – case-by-case basis.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

The AMS for waiver of recurrent salivary stones or fistula should include:

- 1. History, physical (thorough head and neck examination), medical evaluation and treatment for all episodes; to include complete description of presenting symptoms.
- 2. Reference to all laboratory and imaging studies obtained.
- 3. Otolaryngology/oral-maxillary consultation; with specific reference to likelihood of recurrence.
- 4. Statement regarding ability to speak clearly and to adequately fit aviator oxygen mask and other required life support equipment.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

The AMS for an initial waiver for impaired speech or mastication or other condition which precludes wear of life support equipment should include:

- 1. History, physical, medical evaluation and treatment; to include complete description of presenting symptoms.
- 2. Reference to all laboratory and imaging studies obtained.
- 3. Operative notes, if applicable.
- 4. Histology report, if applicable.
- 5. Otolaryngology/oral-maxillary consultation; with specific reference to likelihood of recurrence and/or malignant transformation and need for on-going surveillance.
- 6. Statement regarding ability to speak clearly and to adequately fit aviator oxygen mask and other required life support equipment.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

The AMS for a waiver for a benign tumor should include:

- 1. History, physical, medical evaluation and treatment; to include complete description of presenting symptoms and any residual symptoms after treatment.
- 2. Reference to all laboratory and imaging studies obtained.
- 3. Operative notes (initial waiver only).
- 4. Histology report (initial waiver only). (For rare cell types, a Joint Pathology Center report required.)
- 5. Otolaryngology/oral-maxillary consultation; with specific reference to likelihood of recurrence and/or malignant transformation and need for on-going surveillance.
- 6. Statement regarding ability to speak clearly and to adequately fit aviator oxygen mask and other required life support equipment.
- 7. MEB results if applicable.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

The AMS for a waiver for a malignant tumor should include:

- 1. History, physical, medical evaluation and treatment; to include complete description of presenting symptoms any residual symptoms after treatment.
- 2. Reference to all laboratory and imaging studies obtained.
- 3. Operative notes (initial waiver only).
- 4. Histology report (to include AFIP report) (initial waiver only).
- 5. Medical evaluation board summary recommendations (initial waiver only).
- 6. Otolaryngology and oncology consultation; with specific reference to likelihood of local recurrence or metastasis and detailed description of recommended surveillance regimen.
- 7. Statement regarding ability to speak clearly and to adequately fit aviator oxygen mask and other required life support equipment.
- 8. Tumor board results.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### III. Aeromedical Concerns

Most salivary gland disorders would generally not be considered to pose an immediate risk to flight; at least relative to the risk for sudden incapacitation in flight from a known or yet to be diagnosed condition. Certainly, a salivary stone may cause pain during flight (especially following a meal) but this does not generally produce incapacitating levels of discomfort such as those frequently associated with renal stones. As such, most aeromedical concerns relate to the identification of conditions that might interfere with clear speech, wear of the oxygen mask, or require acute medical intervention such as antibiotic or anti-inflammatory medication use.

A query of AIMWTS through February of 2019 revealed a total of 19 aviator waiver requests for salivary gland disorders. All but five received a waiver. There were 2 FC I/IA cases (0 disqualified), 9 FC-II cases (1 disqualified), 1 RPA pilot case (0 disqualified), 4 FC-III cases (2 disqualified), 2 ATC/GBC cases (1 disqualified), and 1 MOD case (1 disqualified).

| ICD-9 Code | Non-neoplasm Salivary Gland Conditions                                    |
|------------|---|
| 527.5      | Sialolithiasis  |
| 527.6      | Mucoceles   |
| 527.7      | Disturbance of salivary secretion, to include hyposecretion, ptyalism,    |
|            | sialorrhea, and xerostomia  |
| 527.8      | Other specified diseases of the salivary glands (benign                   |
|            | lymphoepithelial lesions, sialectasia, sialosis, stenosis of the salivary |
|            | duct, stricture of the salivary duct)                                     |
| 710.2      | Sicca syndrome (Sjögren's syndrome, keratoconjunctivitis sicca)           |
| 750.23     | Atresia, salivary gland   |
| 750.24     | Congenital fistula of the salivary gland                                  |

| ICD-9 Code | Salivary Gland Neoplasms                             |
|------------|--|
| 142.0      | Parotid gland, malignant neoplasms                   |
| 142.1      | Submandibular gland, malignant neoplasms             |
| 142.2      | Sublingual gland, malignant neoplasms                |
| 142.8      | Other major salivary glands, malignant neoplasms     |
| 142.9      | Salivary gland, unspecified, malignant neoplasms     |
| 210.2      | Major salivary glands, benign neoplasm               |
| 230.0      | Lip, oral cavity, and pharynx, carcinoma in situ     |
| 235.0      | Major salivary gland, neoplasm of uncertain behavior |

| ICD-10 Code | Non-neoplasm Salivary Gland Conditions                |  |
|-------------|---|--|
| K11.5       | ialolithiasis   |  |
| K11.6       | Mucucoele of salivary gland                           |  |
| K11.7       | Disturbance of salivary secretion                     |  |
| K11.8       | Other diseases of the salivary glands                 |  |
| M35.00      | Sicca syndrome, unspecified                           |  |
| Q38.4       | Congenital malformations of salivary glands and ducts |  |

| ICD-10 Code | Salivary Gland Neoplasms   |
|-------------|--|
| C07         | Malignant neoplasm of parotid gland                                  |
| C08.0       | Malignant neoplasm of submandibular gland                            |
| C08.1       | Malignant neoplasms of sublingual gland                              |
| C08.9       | Malignant neoplasm of major salivary gland, unspecified              |
| D11.9       | Benign neoplasm of major salivary gland, unspecified                 |
| D00.0       | Carcinoma in situ of lip, oral cavity, and pharynx                   |
| 235.0       | Neoplasm of uncertain behavior of major salivary glands, unspecified |

## **IV. Suggested Readings**

- 1. Wilson DF, Meier JD, and Ward PD. Salivary Gland Disorders. Am Fam Physician, 2014; 89(6): 882-88. https://www.aafp.org/afp/2014/0601/p882.html
- 2. Fazio SB and Emerick K. Salivary gland stones. UpToDate. Apr 2018. https://www.uptodate.com/contents/salivary-gland-stones?search=Salivary%20gland%20stones&source=search\_result&selectedTitle=1~7&usage\_type=default&display\_rank=1
- 3. Laurie SA. Salivary gland tumors: Epidemiology, diagnosis, evaluation, and staging. UpToDate. Jan 2018. https://www.uptodate.com/contents/salivary-gland-tumors-epidemiology-diagnosis-evaluation-and-

 $staging?search=Salivary\%20 gland\%20 tumors:\%20 Epidemiology,\%20 diagnosis,\%20 evaluation,\%20 and\%20 staging\&source=search\_result\&selectedTitle=1 \sim 34 \&usage\_type=default\&display\_rank=10 glasses.$ 

#### WAIVER GUIDE

Updated: March 2020

Supersedes Waiver Guide of Sept 2015

By: Lt Col John M. Hatfield (RAM 16) and Dr. Dan Van Syoc

Reviewed by Lt Col Dara D. Regn, ACS Pulmonologist

## **CONDITION:**

Sarcoidosis (Mar 2020)

### I. Waiver Consideration.

Sarcoidosis is disqualifying for all flying classes (FC I/IA, II, and III), ATC/GBO, and SWA personnel, as well as retention. Therefore, a waiver and MEB are necessary for these personnel.

History of cardiac or CNS involvement is typically not waiverable. Also sarcoidosis causing hypercalcemia is not compatible with a waiver. Please consult Uveitis Waiver Guide if ophthalmologic sarcoidosis is present.

**Table 1: Waiver potential for sarcoidosis** 

| Flying Class (FC)              | Condition  | Waiver Potential<br>Waiver | ACS review/evaluation             |
|--------------------------------|--|----------------------------|-----------------------------------|
|                                |  | Authority                  |                                   |
| I/IA                           | History of sarcoidosis (asymptomatic or symptomatic) with disease resolution.                            | Maybe*†<br>AETC            | Yes                               |
| Trained II/III ATC/GBO         | Sarcoidosis that is asymptomatic, stable, no treatment required, and no functional impairment.           | Yes#†<br>AFMRA             | Yes, initial waiver or if relapse |
|                                | Sarcoidosis previously treated with steroids and now asymptomatic, stable and no functional impairment.‡ | Yes‡†<br>AFMRA             | Yes, initial waiver or if relapse |
| Untrained<br>II/III<br>ATC/GBO | History of sarcoidosis (asymptomatic or symptomatic) with disease resolution. ‡                          | Maybe*†<br>AFMRA           | Yes                               |

<sup>†</sup> History of cardiac or CNS involvement is typically not waiverable.

AIMWTS search in Sep 2015 revealed a total of 42 cases with the diagnosis of sarcoidosis. Eight (19.5%) were disqualified. There were no FC I/IA cases, 19 FC II cases (1 disqualification), 22 FC III cases (7 disqualifications), 1 ATC case (not disqualified), and no MOD cases.

## II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for sarcoidosis for <u>initial waiver or waiver for recurrent</u> (relapsed) sarcoidosis should include the following:

A. History – occupational (silicates, beryllium) and environmental (moldy hay, birds, TB, coccidioidomycosis, histoplasmosis) exposures, signs, and symptoms (including negative, covering all organ systems), activity level, medications/treatment (if treated with corticosteroids within the

<sup>\*</sup> Waiver considered only if asymptomatic, no functional impairment and remission without treatment for at least 3 years duration.

<sup>#</sup> Waiver for trained aviators requires three-month follow-up to assure stability of newly diagnosed (histologically proven) disease prior to waiver submission.

<sup>‡</sup> If systemic corticosteroid therapy results in remission, then waiver may be submitted after six months off medication if asymptomatic, no evidence of recrudescence and pituitary-adrenal axis has returned to normal function (see Systemic Glucocorticoid (Steroid) Treatment Waiver Guide).

year then Cosyntropin® stimulation test [see Systemic Glucocorticoid (Steroid) Treatment Waiver Guide]).

- B. Complete physical with emphasis on lung, skin, eye, liver and heart, and thorough neurologic examination.
- C. Internal medicine or pulmonologist consultation.
- D. Testing: CXR, biopsy results, full pulmonary function testing with spirometry pre/post bronchodilator, lung volumes, and DLCO, 12-lead ECG and 24-hour Holter monitor test.
- E. Laboratories complete blood count (CBC), calcium, liver function tests, creatinine, blood urea nitrogen (BUN), urinalysis, 24 hour urine creatinine, and 24 hr urine calcium.
- F. TB skin test.
- G. Ophthalmology/optometry exam, to include slit lamp.
- H. MRI with gadolinium. Neurology consultation if symptoms or signs indicate possible involvement.
- I. MEB results.

The AMS for waiver renewal of individuals in continued remission should include the following:

- A. History brief summary of previous signs, symptoms, and treatment, current signs or symptoms (include negative), activity level, and medications.
- B. Physical complete physical, addressing lung, skin, eye, liver, heart, and CNS.
- C. Testing: CXR, full pulmonary function testing with spirometry pre/post bronchodilator, lung volumes, and DLCO.
- D. Laboratories complete blood count (CBC), calcium, liver function tests, creatinine, blood urea nitrogen (BUN), and urinalysis. 24 hour urine calcium and creatinine should also be submitted if previous symptoms or current findings indicate systemic involvement.
- E. Ophthalmology/optometry exam, to include slit lamp.
- F. Neurologic or cardiac evaluation if current findings indicate involvement

#### III. Overview.

Sarcoidosis is a multisystem disorder characterized by the presence of discrete, compact, noncaseating epithelioid granulomata. The typical sarcoid granuloma is found in the lung, distributed along lymphatic chains, but can be found in virtually any organ. Though the precise etiology is unknown, recent evidence demonstrating T-cell lymphocytes layering around the granuloma suggests an immunological reaction in genetically susceptible individuals who are exposed to specific environmental agents.<sup>1-4</sup> There is also newer evidence that there may be an infectious etiology to the condition.<sup>5</sup> The true incidence is unknown; in view of the large proportion of cases that are discovered serendipitously on chest radiographs, it is estimated that only around 20% of sarcoidosis cases are ever found.<sup>2,6,7</sup> Sarcoidosis was once thought to be rare in North America, but beginning in the 1940s increasingly large numbers of cases were identified by chest xray (CXR) screening, particularly by the military. <sup>7,8</sup> The disease most often arises in the third to fourth decades of life, and shows an increased predilection for those of African-American, Caribbean, Japanese, Scandinavian, and Irish descent. The condition tends to wax and wane in its course, with marked variability in the pattern of organ involvement. 2, 3, 6, 9, 10 There also appear to be geographic differences in the prevalence of sarcoidosis, even among populations with similar genetic backgrounds. It has been theorized that this regional variability may be related to environmental exposures.<sup>2</sup>

Most commonly, sarcoidosis presents in one of three ways: as an asymptomatic finding on CXR; with nonspecific constitutional symptoms; or with organ-specific complaints.<sup>2</sup> In various series, 30% to 60% of clinical presentations are asymptomatic and incidentally found, typically with radiographic findings of bilateral hilar adenopathy (BHA), with or without parenchymal opacities.<sup>10</sup> Nonspecific symptoms may include fever, weight loss, fatigue, or muscle weakness. Organ-specific presentations are protean, and may manifest with dermatologic lesions, dyspnea on exertion, cough, vision changes or eye pain, cranial or peripheral nerve palsies, seizures, arthralgia, cardiac conduction blocks or even sudden cardiac death. Due to the variability of symptoms, delay in diagnosis is not uncommon.

The onset of symptoms may be acute. This type of presentation is more common in Caucasians than in African-Americans or Japanese, and may present as Löfgren's syndrome with BHA, ankle arthritis, erythema nodosum (EN) or generalized constitutional symptoms. An acute presentation portends the best prognosis, often resulting in spontaneous remission within two years.

Chronic sarcoidosis, common in African-Americans, often presents with pulmonary symptoms. Constitutional symptoms are less common with the chronic form. This type is often relapsing, with a protracted course and a less favorable prognosis.<sup>2</sup>

Pulmonary involvement: Pulmonary sarcoidosis is a predominantly interstitial lung disease, with symptoms and radiographic findings similar to other fibrotic lung diseases. Prominent symptoms are dyspnea, dry persistent cough, and chest pain. Significant interstitial disease may lead to abnormal pulmonary function and oxygen diffusion capacity. However, in contrast with other interstitial lung diseases such as idiopathic pulmonary fibrosis, profuse radiographic changes are often associated with minimal physiologic alterations in lung function. The granulomatous inflammation, which favors the upper lung fields, tends toward a peribronchial distribution, which helps explain two additional clinical phenomena that are unusual with other interstitial lung diseases: transbronchial biopsy is usually successful in establishing a histologic diagnosis, and some patients (roughly 15%) experience bronchospasm as a complication of the disease. Sarcoidosis has rarely presented with tracheal or laryngeal involvement, hemoptysis, unilateral involvement, pleural effusion, pneumothorax, pleural thickening, cavity formation, calcification of lymph nodes, or clubbing. 13, 14

Even when patients initially present with extrapulmonary manifestations, over 90% have radiographically evident pulmonary involvement. Because pulmonary involvement is nearly ubiquitous, and is the most common cause of sarcoid-related morbidity, staging of sarcoidosis is based on radiological characteristics of the CXR. It is important to note that sarcoidosis normally does not progress though each of the 5 stages in a predictable fashion. Patients with sarcoidosis can present with any stage of disease; and while their disease may go on to progress to another stage, it may also remit or remain stable. The following are the various stages and remission rates: 1, 2, 15

- Stage 0 disease has a normal CXR (which implies extrapulmonary disease is the presenting manifestation or that the disease has remitted).
- Stage I disease is defined by the presence of BHA, which is often accompanied by right paratracheal node enlargement. 50% of affected patients exhibit BHA as the first expression of sarcoidosis. Regression of hilar nodes within one to three years occurs in 75% of such patients, while 10% develop chronic enlargement that can persist for 10 years or more. When BHA is associated with EN, migratory polyarthralgias, and fever, the diagnosis of

- Löfgren's syndrome is highly likely. Patients with stage 1 disease are most often asymptomatic.
- Stage II disease consists of BHA and reticular opacities (the latter occurring in the upper
  more than the lower lung zones). These findings are present at initial diagnosis in 25% of
  patients. Two-thirds of such patients undergo spontaneous resolution, while the remainder
  either have progressive disease or display little change over time. Patients with stage II
  disease usually have mild to moderate symptoms, most commonly cough, dyspnea, fever,
  and/or fatigue.
- Stage III disease consists of reticular opacities with shrinking or absent hilar nodes. Reticular opacities are predominantly distributed in the upper lung zones. This form typically remits in 10-20% of cases.
- Stage IV disease is characterized by fibrotic, reticular opacities with evidence of volume loss, predominantly distributed in the upper lung zones. Conglomerated masses with marked traction bronchiectasis may also occur. Extensive calcification and cavitation or cyst formation may also be seen. Remission occurs in 0-5% of individuals with this stage.

Cardiac involvement: Roughly 5% develop clinically evident cardiac involvement, though autopsy studies of sarcoid patients have reported granulomatous infiltration of the myocardium in 13 to 30% of patients. (It should be borne in mind that, with the exception of cardiac and severe pulmonary disease, sarcoidosis is rarely fatal, and thus myocardial sarcoidosis is almost certainly overrepresented in autopsy series.)<sup>16-18</sup> The left ventricle and interventricular septum are most often involved. 19 In a well-known study of 250 patients with cardiac sarcoidosis who were followed for several years, the following complications were noted: complete heart block (49), premature ventricular contractions and ventricular tachycardia (48), myocardial disease (43), sudden death (37), bundle branch block (33), suprayentricular arrhythmia (23), valvular lesions (21), and pericarditis (6).<sup>20</sup> Other subtle findings may be premature atrial and ventricular contractions, and OT dispersion by ECG.<sup>21</sup> Heart block is most likely due to disease of the AV node or the bundle of HIS.<sup>17</sup> Since healed myocardial granulomata may become foci for abnormal automaticity leading to arrhythmias, patients in remission who have had myocardial involvement remain at risk for sudden death. Before the advent of implantable cardiac defibrillators, several studies of cardiac sarcoid reported a risk of sudden death of 33-67%. 16, 20, 22, 23, 24 Routine ECG, holter monitoring, and transthoracic echocardiogram are routinely used to screen for cardiac sarcoidosis. However, if the diagnosis is suspected, cardiac MRI is the most sensitive imaging modality.

Dermatologic involvement: Cutaneous manifestations of sarcoidosis involve approximately one-third of patients, and can be variable. The classic panniculitis of EN is a common presentation of acute sarcoidosis in Caucasian, Puerto Rican, and Mexican patients and is the least beneficial lesion to biopsy.<sup>2, 11</sup> Other dermatologic lesions include small purplish papules, plaques, or subcutaneous nodules. While these are less distinctive on physical examination, biopsy will often yield a histologic diagnosis of noncaseating granulomata. Small, pink, maculopapular eruptions may wax and wane, may present as scarring sarcoidosis, and may cause alopecia. Sarcoid lesions may invade old scars. On blanching with a glass slide, dermal sarcoid lesions often reveal an "apple jelly" yellowish brown color.<sup>25</sup> As a rule, sarcoid lesions do not itch, ulcerate, or cause pain.<sup>1</sup>

<u>Ocular involvement:</u> In most series, ocular involvement occurs in 25-33% of individuals. As with other granulomatous disorders, sarcoidosis can affect any part of the eye and involvement may or may not be symptomatic. Anterior uveitis is the most common manifestation, often presenting with

ocular pain, redness or changes in vision. Posterior chronic uveitis may be occult and may, over time, lead to secondary glaucoma, cataracts, or blindness.<sup>2</sup> Other eye lesions include conjunctival follicles, dacryocystitis, and retinal vasculitis.<sup>1</sup>

Nervous system involvement: Neurological manifestations can occur in up to 5 to 10% of cases, though one series found neural involvement in 26% of sarcoid patients. <sup>26</sup> Neurosarcoidosis favors the base of the brain, and may present as a cranial nerve palsy (especially facial nerve palsy), panhypopituitarism, fulminant delirium, hydrocephalus or chronic meningitis. <sup>27-29</sup> Seizures have been reported in 5%-22% of neurosarcoidosis patients, but are rarely the presenting symptom. <sup>30</sup> Granulomatous involvement of the hypothalamus may result in defective release of vasopressin, adrenocorticotropic hormone, and glucagon; in particular the defect in vasopressin may lead to diabetes insipidus. <sup>27</sup> These lesions are typically early findings and respond well to treatment. <sup>1</sup> On the other hand, space occupying lesions, seizures, peripheral nerve lesions, and neuromuscular involvement tend to occur as a late manifestation, and most likely indicate chronic disease. <sup>2</sup> MRI imaging often reveals the presence of leptomeningeal enhancement. Cerebrospinal fluid (CSF) findings are nonspecific, and may include lymphocytosis, increased protein, and/or elevated angiotensin-converting enzyme (ACE) levels, lysozymes, increased CD4/CD8 ratios and β-2 macroglobulins. The triad of facial nerve palsy, parotiditis, and anterior uveitis is called the Heerfordt syndrome and, unlike most neural involvement, suggests a favorable prognosis. <sup>1</sup>

<u>Musculoskeletal involvement:</u> It has been estimated that joint pains occur in 25-39% of sarcoid patients, although deforming arthritis is rare. Acute polyarthritis (especially in the ankles) usually occurs in the presence of anterior uveitis or EN. Chronic arthritis may mimic rheumatologic disease, even to the extent of causing a false positive test for rheumatoid factor. <sup>15</sup> Muscular involvement may affect up to 10% of sarcoidosis patients. Proximal muscle weakness, muscle wasting, diaphragmatic weakness, and quadriceps weakness have been described in the literature. <sup>31</sup> Respiratory muscle involvement has very rarely led to respiratory failure. <sup>32, 33</sup>

<u>Lymphatic involvement:</u> Extrathoracic lymphadenopathy is commonly found in the cervical, axillary, epitrochlear, and inguinal chains. Such nodes are typically non-tender and patients are usually unaware of them; their importance is primarily as an easy site for diagnostic biopsy.<sup>1</sup> At the time of autopsy the spleen is involved in 40-80%, but clinically important manifestations of hypersplenism such as anemia or spontaneous rupture are rare.<sup>2</sup>

<u>Gastrointestinal involvement:</u> Although liver biopsy will show sarcoid granulomata in 70% of cases, altered liver function due to granulomatous hepatitis or portal hypertension is rare.<sup>2, 9</sup> (Due to the lack of specificity of hepatic granulomata, the liver is not generally recommended as a biopsy site.) Clinically symptomatic gastrointestinal involvement, which may mimic infectious gastroenteritis, inflammatory bowel disease, tuberculosis, fungal infection or pancreatic neoplasm, affects less than 1% of patients.<sup>1</sup>

Osseous involvement: Lytic or sclerotic bone lesions are present in 10% of cases and are almost always accompanied by chronic skin findings.<sup>2</sup> Bone resorption secondary to endocrine abnormalities with vitamin D, noted below, is integral to the pathogenesis of hypercalciuria.

<u>Endocrine/renal involvement:</u> Disordered calcium metabolism, due to conversion of vitamin D to the active form within granulomata, often results in hypercalciuria with the attendant risk of nephrolithiasis; hypercalcemia is much less common (2-10%).

Quality of life/Emotional implications: One study of 111 sarcoid individuals revealed up to 66% had experienced depression (worse while on steroid treatment) and 55% had increased stress when compared to the average study population without sarcoidosis. These levels are comparable to patients with symptomatic AIDS, end-stage renal disease, and moderate to severe COPD.<sup>34</sup>

The pulmonary literature has vacillated about the need for histologic confirmation of sarcoidosis in the most typical presentation, that of an individual with asymptomatic BHA found on CXR. Since this is a relatively uncommon presentation for lymphoma, some have argued in favor of clinical follow-up rather than proceeding to biopsy. However, current consensus is that histologic confirmation is advisable to confirm sarcoidosis, and to rule out lymphoma and infections such as tuberculosis. For aviators, "watchful waiting" is even more problematic, since it would require grounding for up to twelve months. And regardless of flight status, most patients are anxious to have confirmation of the diagnosis. If physical examination demonstrates involvement of superficial lymph nodes, skin (except EN), conjunctivae, or salivary glands, then biopsy should be directed toward that site. CT scan may prove to be useful for extent of involvement, particularly to delineate mediastinal adenopathy. Transbronchial biopsy has a high yield in Stage 1 and higher disease; even when the disease process appears to be limited to hilar nodes, biopsy of lung tissue is usually positive for non-caseating granulomata. The use of endobronchial ultrasound allows direct sampling of enlarged hilar and mediastinal lymph nodes, further increasing the diagnostic yield of bronchoscopy. Bronchoalveolar lavage, on the other hand, is of limited prognostic value, other than to exclude alternative diagnoses. When flow cytometry analysis is done on the lavage fluid, an elevated CD4/CD8 ratio can suggest sarcoidosis. However, this finding is non-specific and is insufficient to make a definitive diagnosis.<sup>2</sup> As noted earlier, liver biopsy is not recommended. The Kveim test and blind scalene lymph node or fat pad biopsies are obsolete. The ACE level is elevated in 40-90% of individuals with active sarcoidosis; however, a high ACE level is not specific for sarcoidosis, and the magnitude of an initial elevation has no prognostic significance.<sup>8</sup> As cardiac involvement typically has a patchy distribution, cardiac biopsy has low sensitivity (about 20% in one study) and is not recommended, even when there is a high suspicion for myocardial involvement.<sup>17, 35</sup> In general, disease which is isolated to the heart, brain, or eye is not biopsied. The diagnosis is normally based on clinical presentation and characteristic radiographic findings. In the first two cases, such involvement is rarely waiverable anyway. Idiopathic granulomatous uveitis must be evaluated at the ACS, and is generally waiverable only when quiescent (see Uveitis Waiver Guide.)

Only a minority of sarcoidosis patients will actually require therapy. When treatment is necessary, the standard regimen is a prolonged course of oral prednisone, but recommended dosages vary widely. Corticosteroids accelerate clearance of symptoms, physiologic disturbances, and x-ray changes, but it is not clear that long-term prognosis is altered by such therapy. Treatment is indicated for patients with progressive pulmonary disease, cardiac involvement, CNS disease, uveitis, or hypercalcemia. For the 10% who fail to respond to corticosteroids, chlorambucil, leflunomide, azathioprine, hydroxychloroquine, TNF-inhibitors and methotrexate are possible alternative medications.

More than 85% of remissions occur within the first two years. Failure to regress spontaneously within 2 years forebodes a chronic or persistent course.<sup>1,2</sup> Only about 2-8% of those individuals who spontaneously remit or stabilize will relapse at a later date.<sup>3,8</sup> Corticosteroid-induced remissions, on the other hand, have a high rate of relapse, ranging from 14-74%, although one study showed no relapses if individuals remained asymptomatic for three years after prednisone withdrawal.<sup>1,2</sup>

A recent British study has developed a prognostic tool that utilizes a composite physiologic index (CPI) along with high-resolution CT (HRCT) staging system. This is an early tool that offers hope for more successful management decision making.<sup>36</sup>

### IV. Aeromedical Concerns.

The most common aeromedical concerns are typically cardiac and pulmonary, though ophthalmologic and neurologic involvement may also prove to be a hindrance to flight crew duties. Myocardial involvement may present as arrhythmias, conduction block, and syncope leading to sudden incapacitation during flight. Restrictive pulmonary disease is itself an aeromedical concern, particularly if blood gases are affected or airway hyper-reactivity is present. A crewmember with stage II or III sarcoidosis may have altered oxygen diffusion, thus exacerbating or accelerating symptoms of hypoxia and reduced decision making abilities at altitude. Reductions in FVC and FEV1 may accompany sarcoidosis even with optimized medical management.

CNS disease (e.g., cranial nerve palsies, encephalopathy, seizures), depression, ocular complications (e.g., uveitis, iritis, chorioretinitis), and renal calculi all have direct aeromedical implications. Neuromuscular involvement, especially of proximal muscle groups (and the predilection towards quadriceps muscle group involvement), have important implications for rudder control and anti G-straining maneuvers.

No individual should fly while undergoing treatment. Steroid treatment itself has a variety of metabolic, psychiatric, and CNS effects which may make flying hazardous.<sup>10</sup>

| ICD-9 code for Sarcoidosis |             |
|----------------------------|-------------|
| 135                        | Sarcoidosis |

| ICD-10 code fo | or Sarcoidosis           |
|----------------|--------------------------|
| D86.9          | Sarcoidosis, unspecified |

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# Seizures, Epilepsy, and Abnormal EEG (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Updated Table 1 and References

### I. Waiver Consideration

Medical standards for appointment, enlistment and induction state that epilepsy occurring beyond the 6th birthday is disqualifying, unless the applicant has been free of seizures for a period of 5 years while taking no medication for seizure control, and has a normal electroencephalogram (EEG). Childhood seizures are addressed by stating that "seizures associated with febrile illness before 5 years of age may be acceptable with waiver if recent neurological evaluation, MRI, and EEG including awake and sleep samples are normal". Childhood seizures with prolonged remission may be amenable to waiver consideration on an individual basis. Truly provoked seizures may also be aeromedically-acceptable for waiver consideration on an individual basis. Unprovoked seizures are generally not recommended for waiver due to unacceptably-high recurrence risk. For information on post-traumatic seizures and waiver potential, please consult the Waiver Guide chapter on traumatic brain injury.

For aviators with isolated epileptiform EEG abnormalities and no history of seizure or epilepsy, clinical surveillance is indicated, with categorical waiver recommendation for at least one year, based on data that most non-epileptic adult patients with isolated epileptiform EEG abnormalities who develop seizures will do so within one year of EEG abnormality identification.

Table 1: Waiver potential for seizures, epilepsy and abnormal (epileptiform) EEG findings

| Flying Class (FC)     | Waiver Potential   | Waiver Authority | ACS Review or Evaluation |
|-----------------------|--------------------|------------------|--------------------------|
| FC I/IA               | Yes <sup>1</sup>   | AFMRA            | Yes                      |
| FC<br>II//III/SWA/OSF | Yes <sup>1,2</sup> | AFMRA            | Yes                      |
| ATC/GBO               | Yes <sup>1</sup>   | AFMRA            | Yes                      |

<sup>1.</sup> Waiver usually not recommended for unprovoked seizures or epilepsy. Cases of isolated EEG abnormalities without seizures may be acceptable for waiver on a case-by-case basis after careful review by an epileptologist.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable. The diagnosis of a seizure is still primarily clinical, and every effort must be made to try and reconstruct what happened before, during and after a suspected seizure event. Special attention should be paid to clinical notes from all who had contact with the patient, such as medical technicians, paramedics, nurses, emergency department personnel, and providers. The medical history should address the relevant period preceding and during the suspected event and include a review of travel, sleep, diet, work and all medications,

<sup>2.</sup> Isolated EEG abnormalities not disqualifying for OSF duty.

whether prescription or over-the-counter. Any ethanol, caffeine and nicotine intake should be listed. Accounts from witnesses must be included in the medical record, either as a written statement from the eyewitness, or as an account documented by a provider. If written accounts were not accomplished initially, then every effort should be made to identify possible witnesses and include their accounts.

# A. <u>Initial Waiver Request:</u>

- 1 Historical details as listed above.
- 2 Reports of consultations and diagnostic testing, including: neurology consultations, neuroimaging studies (MRI reports and images), laboratory testing, and EEG reports. Recent brain MRI and EEG studies are needed in cases of remote seizures. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical, mental status and neurologic examination findings.
- 4 Neuropsychological testing if performed. Contact ACS Neuropsychology for questions or further guidance on need for testing and on which tests to administer.
- 5 RILO/MEB results, if obtained.
- If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical, mental status and neurologic examination findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual neurologic or cognitive symptoms and signs and any medication effects on operational safety and mission effectiveness, and future risk of seizure occurrence, with resulting sudden incapacitation. For unprovoked seizures in adults, the risk of recurrence is greater than 40% over five years. This aeromedically-unacceptable risk is further increased with other factors such as prior brain lesion or insult causing the seizure, an EEG with epileptiform abnormalities, a significant brain imaging abnormality and nocturnal seizure occurrence. Truly provoked seizures may be amenable to waiver consideration on an individual basis. Sleep deprivation alone is not considered a provocative factor for seizures in neurologically intact individuals. Children with a nonfebrile unprovoked seizure and a normal EEG have a fiveyear recurrence rate of about 21% and recurrences after that time frame are not common. Absence seizures have a repeat seizure rate of 42% over the next 25 years (to include other types of seizures) and are therefore permanently disqualifying. Children with simple febrile seizures generally do not have significant risk for seizure recurrences in adulthood and this diagnosis is amenable to waiver consideration. Brain MRI with attention to medial temporal lobe structures ("seizure protocol") is the most appropriate imaging study to obtain. EEG studies are needed in diagnostic evaluation. These do not prove or disprove the diagnosis of epilepsy, although an unequivocally abnormal EEG combined with a clinical history compatible with seizure does support the diagnosis. However, EEG studies can be completely normal in known epileptic patients, and a small percentage of the normal population will have apparent epileptiform patterns on EEG. A 1968 review of non-epileptic patients with epileptiform changes on EEG showed that the vast majority of adult patients who developed seizures did so within 12 months of discovery of the EEG abnormalities. In such cases, observation with restricted aviation duties and follow-up EEG studies are usually recommended to determine if a less restrictive waiver might be safely considered in the future. No anticonvulsant medications are aeromedically-approved for use in USAF aviators for management of seizures, although gabapentin and topirimate are approved for use in MOD personnel for non-epilepsy conditions such as pain and migraine.

AIMWTS search in Jan 2019 revealed 329 cases. Breakdown of the cases was as follows: 73 FC I/IA cases (29 disqualified); 84 FC II cases (46 disqualified); 10 RPA pilot cases (1 disqualified), 108 FC III cases (62 disqualified); 34 ATC/GBC cases (24 disqualified); and 20 MOD cases (12 disqualified). The vast majority of the approved cases were for childhood febrile seizures with several provoked seizures as well.

| ICD-9 codes for seizures |                                 |  |
|--------------------------|---------------------------------|--|
| 345                      | Epilepsy                        |  |
| 780.3                    | Convulsions                     |  |
| 780.31                   | Simple febrile convulsions      |  |
| 780.32                   | Complex febrile convulsions     |  |
| 780.33                   | Post traumatic seizures         |  |
| 780.39                   | Other (unspecified) convulsions |  |

| ICD-10 codes for seizures |  |  |
|---------------------------|--|--|
| G40.919                   | Epilepsy, unspecified, intractable, without status epilepticus |  |
| R56.00                    | Simple febrile convulsions                                     |  |
| R56.01                    | Complex febrile convulsions                                    |  |
| R56.1                     | Post traumatic seizures  |  |
| R56.9                     | Unspecified convulsions  |  |
| R94.01                    | Abnormal EEG   |  |

# **IV. Suggested Readings**

- 1. Schachter SC. Evaluation and management of the first seizure in adults. UpToDate, Aug 11, 2019.
- 2. Millichap JJ. Treatment and prognosis of febrile seizures. UpToDate, Dec 20, 2018.
- 3. Bergey GK. Management of a First Seizure. Continuum: Lifelong Learning in Neurology, 2016; 22(1): 38-50
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- 6. Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2015; 84(16):1705-13.
- 7. Ropper AH, Samuels MA, Klein JP (Ed). Epilepsy and other seizure disorders. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:318-356.
- 8. Lawn L et al. Are seizures in the setting of sleep deprivation provoked? Epilepsy & Behavior 2014; 33:122-125.
- 9. Benbadis SR. "Just like EKGs!" Should EEGs undergo confirmatory interpretation by a clinical neurophysiologist? Neurology 2013; 80 (Suppl 1):S46-S51.
- 10. Salinsky M, Kanter R, Dasheiff RM. Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operational curve. Epilepsia 1987; 28(4):331-334.
- 11. Robin JJ, Tolan GD, and Arnold JW. Ten-Year Experience with Abnormal EEGs in Asymptomatic Adult Males. Aviat Space Environ Med 1978; 49:732-36.
- 12. Zivin L and Marson A. Incidence and Prognostic Significance of "Epileptiform" Activity in the EEG of Non-Epileptic Subject. Brain 1969; 91:751-78.

### Sickle Cell Disease/Trait & Heterozygous Sickling Disorders (Feb 2019)

Authors/Reviewers: Dr. Christopher Keirns, Maj Laura Bridge, and Capt Luke Menner (ACS Internal Medicine); Dr. Dan Van Syoc (Deputy Chief, ACS), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** Clarification of initial certification requirements for flying class (I/IA, II and III) physicals via PEPP. Clarification that individuals with sickle cell trait require an aeromedical waiver and AMS submission only if they have a history of symptoms attributable to sickle cell trait.

### I. Waiver Consideration

Homozygous sickle cell disease (Hb SS), a history of symptomatic sickle cell trait (Hb AS), or heterozygosity with another mutant beta globin allele such as sickle- $\beta$  thalassemia (Hb S- $\beta$ ° thal), sickle cell-hemoglobin C disease (Hb SC), and sickle- $\beta$ + thalassemia (Hb S- $\beta$ + thal) are disqualifying for all flying and special operational duties as well as retention. All initial flying class physical examinations require documented sickle cell screening and if positive, further characterization with hemoglobin electrophoresis. Asymptomatic Hb AS confirmed on hemoglobin electrophoresis does not require an aeromedical waiver. However, EITHER the absence of symptoms commonly associated with a sickling disorder OR presence of symptoms attributable to intravascular sickling MUST be annotated on the initial flight physical prior to certification by the proper authority. Hb SS, Hb SC, Hb S- $\beta$ ° thal, Hb S- $\beta$ + thal, and a history of symptomatic Hb AS are not thought to have aeromedical waiver potential in the manned aviation environment. Waiver for ATC and GBO personnel with a history of symptomatic Hb AS may be considered on a case-bycase basis following accession or retention determination.

Table 1: Waiver potential for Hb SS, Hb SC, Hb S- $\beta$ ° thal, Hb S- $\beta$ + thal, and symptomatic Hb AS

| Flying Class (FC) | Waiver Potential    | Waiver Authority    | ACS Review or Evaluation |
|-------------------|---------------------|---------------------|--------------------------|
| FC I/IA           | No <sup>1</sup>     | AETC                | No                       |
| FC II/III/SWA     | No <sup>1,2,3</sup> | MAJCOM <sup>4</sup> | No <sup>5</sup>          |
| GBO/ATC           | No <sup>1,3</sup>   | MAJCOM              | No <sup>5</sup>          |

<sup>1.</sup> Asymptomatic sickle cell trait (Hb AS) is not disqualifying. However, either the absence of symptoms associated with a sickling disorder or presence of symptoms attributable to intravascular sickling MUST be annotated on the initial flight physical prior to certification by the proper authority. See below for the additional information required for initial physical certification.

- 2. No waiver potential for FC II, FC III, and SWA personnel.
- 3. Waiver for ATC and GBO personnel with history of symptomatic Hb AS may be considered on a case-by-case basis following accession or retention determination.
- 4. Initial FC II and FC III exams treated similarly to FC I/IA.
- 5. ACS review may be requested at the discretion of the waiver authority when waiver consideration is being given to ATC or GBO personnel with a history of symptomatic Hb AS.

### **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations. The following evaluation is required for <u>ALL</u> service members with sickle cell trait (Hb AS) prior to initial certification of flying class (I/IA, II, and III)

physicals via PEPP. <u>ONLY</u> those individuals found to have Hb SS, Hb SC, Hb S- $\beta$ ° thal, Hb S- $\beta$ + thal, and <u>symptomatic</u> Hb AS require AMS submission.

## A. Initial Waiver Request:

- 1. Information to include in history:
  - a. Complete history of symptoms with report of any symptomatic vaso-occlusive episodes, episodes of abdominal pain, hematuria, or renal dysfunction, and any history of rhabdomyolysis, splenic infarct, and/or sudden death with prolonged physical activity (e.g., military boot camp, training for athletic competition)
  - b. Complete list of all therapies, current medications with dates of initiation, doses, and all adverse effects
- 2. Consultation reports from all treating providers or specialists during symptomatic episodes:
  - a. Consultation report from a hematologist should be included if the diagnosis is uncertain
- 3. Laboratory studies required:
  - a. CBC, BMP, urinalysis, and hemoglobin electrophoresis
  - b. All other laboratory and imaging studies ordered by consulting specialist(s), if performed
- 4. Current physical examination findings.
- 5. Any other pertinent information.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### B. Renewal Waiver Request:

- 1. Updated AMS with interval history, including:
  - a. Subjective symptoms with specific comment on any interval symptomatic vaso-occlusive episodes.
  - b. Complete list of all therapies, current medications with dates of initiation, doses, and all adverse effects
- 2. All clinical notes and consultation reports from treating providers or specialists during symptomatic episodes (if applicable)
- 3. Laboratory studies required:
  - a. Updated CBC, BMP, and urinalysis
  - b. All other laboratory and imaging studies ordered by treating providers or consulting specialist(s) related to the diagnosis of hemoglobinopathy, if performed
- 4. Current physical examination findings.
- 5. Any other pertinent information.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Homozygous sickle cell disease (Hb SS), sickle cell trait (Hb AS), and heterozygosity with another mutant beta globin such as sickle- $\beta$  thalassemia (Hb S- $\beta$ ° thal), sickle cell-hemoglobin C disease (Hb SC), and sickle- $\beta$ + thalassemia (Hb S- $\beta$ + thal) are conditions that present aeromedical safety concerns in aviation and austere environments. Hb AS is the only condition that is thought to possess aeromedical waiver potential. With rare exception, Hb AS is not associated with increased risk of intravascular sickling and is not predicted to pose significant aeromedical risk. However, it is

still imperative for the flight surgeon to educate aircrew and special duty operators about this condition and specifically emphasize the importance of hydration before rigorous activities.

Until 1982, individuals with Hb AS were restricted from entering military flight training or performing aircrew duties, and they were barred from attendance at the US Air Force Academy due to the rare occurrences of intravascular sickling under conditions of physiologic stress. Specifically, case reports have demonstrated an association of increased rates of intravascular sickling in individuals with Hb AS when placed in settings of dehydration, hypoxia, and/or strenuous exercise. In 1985, the Secretary of Defense ordered that "all military occupational restrictions on sickle cell trait be removed." This decision was considered appropriate, because the majority of individuals with Hb AS remain asymptomatic. In contrast to Hb SS and other heterozygous sickling disorders, Hb AS is a relatively benign condition with a better clinical course and more favorable prognosis. The lower percentage of abnormal hemoglobin molecules in Hb AS relative to other hemoglobinopathies result in less association with anemia, a less pronounced decrease in red blood cell survival, and normal or near-normal life expectancy. In contrast, Hb SS and other heterozygous sickling disorders are associated with a worse prognosis and commonly results in more significant anemia, a more pronounced shortening of red blood cell survival, and reduced life expectancy compared to a healthy control population.

In general, current Air Force guidance allows individuals with Hb S to access, provided that the proportion of Hb S is less than or equal to 45%. When the percentage of Hb S exceeds 45%, it is indicative of an underlying Hb SS and/or other heterozygous sickling disorder. These individuals are barred from accession to the military because the risk of adverse clinical outcomes is thought to exceed the threshold for military service. The following table summarizes the patterns of electrophoresis in the most common hemoglobinopathies:

Table 2: Adult hemoglobinopathy patterns<sup>1</sup>

| Condition              | Hb A (%) | Hb S (%)  | Hb C (%) | Hb F (%) | Hb A2 (%) |
|------------------------|----------|-----------|----------|----------|-----------|
| Normal (Hb AA)         | 95-98    | 0         | 0        | <2       | 2-3       |
| Sickle cell trait      | 50-60    | $35-45^2$ | 0        | <2       | <3.5      |
| (Hb AS)                |          |           |          |          |           |
| Sickle-β+ thalassemia  | 5-30     | 65-90     | 0        | 2-10     | >3.5      |
| (Hb S-β+ thal)         |          |           |          |          |           |
| Sickle-β thalassemia   | 0        | 80-92     | 0        | 2-15     | >3.5      |
| (Hb S-β° thal)         |          |           |          |          |           |
| Sickle-hemoglobin C    | 0        | 45-50     | 45-50    | 1-5      | <3.5      |
| disease (Hb SC)        |          |           |          |          |           |
| Homozygous sickle cell | 0        | 85-95     | 0        | 5-15     | <3.5      |
| disease (Hb SS)        |          |           |          |          |           |

<sup>1.</sup> Numbers indicate the percent of total hemoglobin in an untransfused adult patient. Ranges are approximate and may vary depending upon the particular laboratory and assay.

Review of AIMWTS data in Feb 2019 revealed 74 members containing the diagnosis of sickle cell disease/trait. Of that total, 15 were FC I/IA (1 disqualified), 8 were FC II (1 disqualified), 3 were RPA pilots, 39 were FC III (7 disqualified), 7 were ATC/GBC (2 disqualified), and 2 were MOD (1 disqualified). Of the 12 disqualifications, only 2 were disqualified specifically for symptomatic Hb AS.

| Common ICD-9 codes used for Sickle Cell Disease/Trait |                             |  |  |
|---|-----------------------------|--|--|
| 282.41/282.42   | Sickle cell thalassemia     |  |  |
| 282.5   | Sickle cell trait           |  |  |
| 282.60/282.61/282.62                                  | Sickle cell disease         |  |  |
| 282.63/282.64   | Sickle cell/Hb-C disease    |  |  |
| 282.68/282.69   | Other sickle cell disorders |  |  |

| Common ICD-10 codes used for Sickle Cell Disease/Trait |                                    |  |
|--|------------------------------------|--|
| D57.0  | Sickle cell disease with crisis    |  |
| D57.1  | Sickle cell disease without crisis |  |
| D57.2  | Sickle cell/Hb-C disease           |  |
| D57.3  | Sickle cell trait                  |  |
| D57.4  | Sickle cell thalassemia            |  |
| D57.8  | Other sickle cell disorders        |  |

### IV. Suggested Readings

- 1. Centers for Disease Control (CDC) Sickle Cell "Toolkit" and Informational Pages: <a href="http://www.cdc.gov/ncbddd/sicklecell/toolkit.html">http://www.cdc.gov/ncbddd/sicklecell/toolkit.html</a> and <a href="http://www.cdc.gov/ncbddd/sicklecell/traits.html">http://www.cdc.gov/ncbddd/sicklecell/traits.html</a>
- 2. National Athletic Trainers' Association Consensus Statement on Sickle Cell Trait and the Athlete: <a href="https://www.nata.org/sites/default/files/SickleCellTraitAndTheAthlete.pdf">https://www.nata.org/sites/default/files/SickleCellTraitAndTheAthlete.pdf</a>

<sup>2.</sup> Percent Hb S can be as significantly lower in patients with sickle cell trait and concomitant alpha thalassemia.

# Sinusitis (Rhinosinusitis), Hypertrophic Sinus Tissue, & Nasal Polyps (Apr 2019)

Reviewed: Major Joshua Shields (RAM), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), Lt Col Wesley Abadie (AF/SG Otolaryngology Consultant), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated format

#### I. Waiver Consideration

A viral URI or episode of acute bacterial rhinosinusitis requires no waiver but is grounding for flyers until resolution. However, chronic sinusitis resulting in clinical symptoms or need for surgical intervention is disqualifying for FC I/IA, II, III, and OSF duties. Nasal polyps that result in symptoms incompatible with flight or altitude chamber duties is disqualifying for FC I/IA, FC II, FC III, OSF, and SWA duties. In addition, any surgical procedure for sinusitis, polyposis or hyperplastic tissue is disqualifying for FC I/IA. For retention purposes, sinusitis that is severe and chronic, either causing frequent missed duty or requiring ongoing ENT follow-up more than annually is disqualifying.

Table 1: Waiver potential for chronic sinusitis, nasal polyps and/or surgery for same

| Flying Class (FC)        | Condition  | Waiver Potential              | ACS Review/             |
|--------------------------|--|-------------------------------|-------------------------|
| Trying Class (FC)        | Condition  | Waiver Authority              | Evaluation <sup>4</sup> |
| I/IA/untrained<br>II/III | Nasal polyps controlled with nasal steroids and/or approved oral antihistamines.   | Yes <sup>2</sup><br>AETC      | No                      |
|                          | Chronic sinusitis controlled with nasal steroids and/or approved oral antihistamines.  | Maybe <sup>2</sup><br>AETC    | No                      |
|                          | Chronic sinusitis, nasal polyps  | Maybe <sup>1</sup><br>AETC    | No                      |
| II/III                   | Nasal polyps controlled with or without nasal steroids and/or approved oral antihistamines.                                    | Yes <sup>2</sup><br>MAJCOM    | No                      |
|                          | Chronic sinusitis controlled with nasal steroids and/or approved oral antihistamines.  | Yes <sup>2, 3</sup><br>MAJCOM | No                      |
|                          | Chronic sinusitis, nasal polyps  | Yes <sup>2, 3</sup><br>MAJCOM | No                      |
| ATC/GBO/ SWA             | Disease severe enough to interfere with enunciation or clear voice communication, or disease that is not responsive to therapy | No<br>MAJCOM                  | No                      |

<sup>1.</sup> Waiver may be considered if at least 12 months after surgery and symptoms entirely resolved.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

The aeromedical summary for <u>initial waiver</u> for nasal polyps should include the following:

- 1. History symptoms (flying and on ground), duration, and treatment.
- 2. Physical HEENT.
- 3. Otolaryngology consultation report.

<sup>2.</sup> Waiver in any untrained candidate requires at least 12 months of symptoms controlled on medication before waiver.

<sup>3.</sup> Altitude chamber ride up to 8-10,000ft with rapid decompression is required. If treated with surgery, altitude chamber ride no earlier than 6 weeks after surgery or when cleared by otolaryngology physician (whichever is later). Exception: a chamber ride is not necessary if the otolaryngologist can visualize the ostia of the affected sinuses or a recent CT shows them to be patent

<sup>4.</sup> ACS review not required, but can be requested on a case-by-case basis.

4. If the local base cannot provide any of the above listed information, they should document why, explaining reason to the waiver authority.

The aeromedical summary for <u>initial waiver</u> for chronic sinusitis and/or surgery should include the following:

- 1. History symptoms (flying and on ground) with duration and frequency, exacerbating factors, and treatment.
- 2. Physical HEENT.
- 3. Otolaryngology consultation report.
- 4. CT scan, showing sinus disease or obstructed anatomy.
- 5. Altitude chamber flight, unless ENT can visualize the ostia of the affected sinuses or a recent CT shows them to be patent.
- 6. Results of MEB or worldwide duty evaluation (for ARC members), if required.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reason to the waiver authority.

The aeromedical summary for <u>waiver renewal</u> of chronic sinusitis, nasal polyps and/or surgery should include the following:

- 1. History symptoms (flying and on ground), treatment, exacerbations since last waiver.
- 2. Physical HEENT.
- 3. Otolaryngology and/or allergy consultation (if symptoms have recurred).
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reason to the waiver authority.

#### **III. Aeromedical Concerns**

Inflammation of the nose and paranasal sinuses is called rhinosinusitis. Infections lasting longer than three months are classified as chronic rhinosinusitis (CRS). Acute and chronic sinusitis and nasal polyps may only be minimally symptomatic at ground level. However, these conditions can block the airflow in and out of the sinus cavities and changes in atmospheric pressure, as seen in the aviator or scuba diver may cause barotraumatic sinusitis, sinus "block" or "squeeze," resulting in sudden, incapacitating pain. These symptoms in aviators normally occur on descent, but rarely have been described on ascent. Should that event occur immediately prior to or during landing procedures, it could lead to sudden incapacitation and an aircraft mishap. There is no quick test to ensure the osteomeatal complex is patent; being able to Valsalva does not ensure aeration of the sinus cavities. One method of ensuring patency after treatment is to expose the aviator to an altitude chamber ride up to 8-10,000 feet. Another is if the operating surgeon can visualize the ostia of the affected sinuses or a recent post-op CT shows them to be patent. Our Air Force consultants strongly encourage doing both tests, rather than to choose one over the other (for complex cases, referral to a rhinologist may be prudent). Oral steroids can be used in the peri-operative period in setting of sinonasal polyposis. Medications used for management may not be compatible with aviation duties: refer to the latest edition of the approved aircrew medication list.

AIMWTS search in Feb 2019 revealed 369 cases with the diagnosis of nasal polyps, chronic sinusitis and/or surgery for the same. Breakdown of cases were as follows: There were 55 FC I/IA cases (9 disqualified), 181 FC II cases (7 disqualified), 9 RPA pilot cases, 120 FC III cases (25 disqualified), 3 ATC/GBC cases, and 1 MOD case.

| ICD9 Codes for Sinusitis, Nasal Polyps and Surgery |                               |  |
|--|-------------------------------|--|
| 473.9  | Unspecified chronic sinusitis |  |
| 471.9  | Unspecified nasal polyps      |  |
| 22.5   | Other nasal sinusotomy        |  |

| ICD10 Codes for Sinusitis, Nasal Polyps and Surgery |   |  |
|---|---|--|
| J32.9   | Chronic sinusitis, unspecified                                      |  |
| J33.9   | Nasal polyp, unspecified  |  |
| 09CP4ZZ   | Extirpation of Matter from Accessory Sinus, Percutaneous Endoscopic |  |
|   | Approach  |  |

# **IV. Suggested Readings**

- 1. Patel, Z., Acute sinusitis and rhinosinusitis in adults: Clinical Manifestations and diagnosis. UpToDate. Sept 2018
- $2.\ Patel,\ Z.,\ Uncomplicated\ acute\ sinusitis\ and\ rhinosinusitis\ in\ adults:\ Treatment.\ Up To Date.\ Sept\ 2018$
- 3. Hamilos, D., Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis. UpToDate. Sept 2018
- 4. Hamilos, D., Chronic rhinosinusitis: Treatment. UpToDate. Sept 2018
- 5. Rosenfeld, R., Clinical Practice Guideline: Adult Sinusitis. Entnet.org. April 2015

#### WAIVER GUIDE

Updated: Mar 2017

Supersedes Waiver Guide of Oct 2015

By: LtCol Dara Regn (ACS pulmonologist), Dr. Chris Keirns, and Dr Dan Van Syoc

### **CONDITION:**

Sleep Disorders (Mar 2017)

#### I. Waiver Consideration.

Narcolepsy, obstructive sleep apnea and other sleeping disorders are disqualifying for all flying classes (FC I/IA, III, SWA, ATC, and GBO). Current or history of sleepwalking is disqualifying for all flying classes (primarily an accession issue), and is unsuiting rather than unfitting for continued military service. Of note, moderate or severe sleep apnea requiring CPAP and OSA incompletely treated with other modalities are considered disqualifying for retention standards, which means that personnel fitting this description will require an I-RILO as well.

As noted earlier, the initial diagnostic workup need not be performed at Wilford Hall or the 88<sup>th</sup> MDG, although this is certainly encouraged where geographically practical. If at all feasible, the initial polysomnogram should be performed at an academic laboratory. In a recent review of ACS experience with OSA, academic laboratory values were concordant with our reference laboratory in 89% of cases, whereas non-academic laboratories were concordant in only 24% of cases. Any FC II aviator other than flight surgeons, with a documented sleep disorder will require an ACS evaluation prior to returning to flying status. FC III individuals and flight surgeons will be seen on a case-by-case basis at the ACS at MAJCOM request (this pertains almost exclusively to Air Battle Managers).

For a waiver to be recommended, the patient must 1) be using a form of therapy that has been documented to be effective on polysomnography testing (repeat PSG showing RDI of <5 with dental orthotic, weight loss, or CPAP), 2) have resolution of sleep-related symptoms, and 3) demonstrate excellent compliance (CPAP usage on 90% of nights for at least 5 hours per night, on average). Generally speaking, all those utilizing CPAP therapy MUST demonstrate a pattern of excellent compliance for at least 30 consecutive days, prior to being granted a waiver. In order to reduce the time required to RTFS, FC II individuals who will require ACS evaluation may submit waiver packages before 30 days of compliance has been documented. However, the patients will still be required to demonstrate a pattern of ongoing usage of at least 30 consecutive days at the time of their ACS evaluation (updated usage data will be downloaded during their ACS evaluation). At the ACS, maintenance of wakefulness testing will be performed on all cases, while neuropsychological testing will be performed only on those with severe sleep apnea. Neither of these tests need to be performed locally prior to waiver submission.

Table 1: Waiver potential for various sleep disorders.

| Flying Class (FC)         | Condition   | Waiver Potential<br>Waiver Authority | ACS review/evaluation     |
|---------------------------|---|--------------------------------------|---------------------------|
| I/IA                      | Sleep walking                                     | Maybe+<br>AETC                       | No                        |
|                           | Narcolepsy  | No<br>AFMRA                          | No                        |
|                           | Obstructive sleep apnea and other sleep disorders | No<br>AETC                           | No                        |
| II (other than FS)        | Sleep walking                                     | Maybe+<br>AFMRA                      | No                        |
|                           | Narcolepsy  | No<br>AFMRA                          | Yes#                      |
|                           | Obstructive sleep apnea                           | Yes*†<br>MAJCOM%                     | Yes#                      |
|                           | Other sleep disorders                             | Maybe<br>MAJCOM%                     | Yes#                      |
| III and FS (FC II)<br>SWA | Sleep walking                                     | Maybe+<br>AFMRA                      | No                        |
|                           | Narcolepsy  | No<br>AFMRA                          | Yes, probable review only |
|                           | Obstructive sleep apnea                           | Yes*†&<br>MAJCOM%                    | Maybe                     |
|                           | Other sleep<br>Disorders                          | Maybe<br>MAJCOM%                     | Yes, probable review only |
| ATC/GBO                   | Sleep walking                                     | Maybe+<br>AFMRA                      | No                        |
|                           | Narcolepsy  | No<br>AFMRA                          | No                        |
|                           | Obstructive sleep apnea                           | Yes&<br>MAJCOM%                      | No                        |
|                           | Other sleep<br>Disorders                          | Maybe<br>MAJCOM%                     | No                        |

<sup>+</sup> Last episode of sleepwalking must be at least three years prior to application with normal psych evaluation. I-RILO may be required if not administratively separated for all sleepwalking cases.

<sup>\*</sup> Mild or moderate OSA documented at ACS with resolved symptoms, good compliance, and normal MWT is waiverable. Severe OSA may also be waiverable, but must also demonstrate normal neuropsych testing.

<sup>#</sup> ACS evaluation includes polysomnography, actigraphy and multiple sleep latency testing (for narcolepsy) or maintenance of wakefulness testing (for OSA) at Wright-Patterson Medical Center Sleep Disorders Laboratory, and may include neuropsychologic testing to evaluate cognitive function.

<sup>&</sup>amp; The only FC III cases seen routinely at the ACS will be Air Battle Managers for the evaluation of possible obstructive sleep apnea. Other aviators do not require ACS review unless requested by the waiver authority.

<sup>†</sup> Indefinite waivers will not be granted for OSA.

<sup>%</sup> AFMRA retains waiver authority for moderate or greater OSA, or clinical sleep disorders that result in excessive daytime somnolence or interfere with duty performance (following I-RILO).

Review of AIMWTS in Mar 2017 showed 18 cases of Narcolepsy, all disqualified. The breakdown of cases was as follows: 1 FC I case, 1 FC II case, 9 FC III cases, 3 ATC/GBC cases, and 4 MOD cases.

Review of AIMWTS showed 124 cases of Sleep Walking and Other Sleep Disorders. Breakdown was as follows: 25 FC I cases (8 disqualifications), 33 FC II cases (8 disqualification), 3 RPA pilot cases (0 disqualified), 46 FC III cases (30 disqualifications), and 7 MOD case (4 disqualifications).

Review of AIMWTS for OSA showed 1321 cases. Breakdown was as follows: 10 FC I/A cases (9 disqualification), 509 FC II cases (102 disqualifications), 9 RPA pilot cases (1 disqualification), 551 FC III cases (148 disqualifications), 151 ATC/GBC cases (29 disqualifications), and 91 MOD cases (19 disqualifications).

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations. Include I-RILO or MEB if required per current MSD.

The aeromedical summary <u>for initial waiver</u> for sleep disorders other than sleep walking should include the following:

A. History – history of weight since reaching adulthood, symptoms (including pertinent negatives), treatment and effectiveness (Epworth score pre and post treatment), and documentation of resolution of symptoms, if applicable. Co-morbidities that exacerbate excessive daytime somnolence in the setting of OSA to include: depression, BMI, sleep duration (bedtime/wake time) and smoking history should be included in the waiver submission. Clinical notes documenting the face-to-face clinical evaluations by the treating sleep physician must also be included.

- B. Physical height and weight, BMI, blood pressure, neck circumference, and ear, nose and throat, cardiovascular, and pulmonary exam.
- C. Polysomnography results [Diagnostic and Treatment (to include formal in lab CPAP titration)]. RDI will be used to determine OSA severity.
- D. I-RILO results, if completed.
- E. If treatment with a PAP device, objective evidence of acceptable adherence to use (usage on 90% of nights for at least 5 hours per night, on average).

The aeromedical summary for <u>waiver renewal</u> for sleep disorders other than sleepwalking should include the following:

- A. History brief summary of initial symptoms, weight and findings at ACS evaluation, current symptoms (including Epworth score), current treatment, and weight history since previous waiver granted. Clinical notes documenting the face-to-face clinical evaluations by the treating sleep physician must also be included.
- B. Physical height and weight, BMI, blood pressure, neck circumference, and ear, nose and throat, cardiovascular, and pulmonary exam.
- C. Polysomnography results. RDI will be used to determine OSA severity. Note: Polysomnography does not need to be accomplished if ACS evaluation is required, will be done during ACS evaluation.
- D. If treatment with a PAP device, objective evidence of acceptable adherence to use (usage on 90% of nights for at least 5 hours per night, on average).

The aeromedical summary for waiver for history of sleepwalking should include the following: A. History – age on onset, frequency, last episode, activities during sleepwalking, family history. B. Psychology/psychiatric consult.

### III. Overview.

The common thread running through most sleep disorders is insufficient quantity or quality of sleep, which leads to excessive daytime sleepiness and diurnal impairment of alertness and cognitive function. While pathologic sleep disorders command the greatest attention, the commonest causes of excessive sleepiness are actually physiologic, such as poor sleep hygiene and circadian shifting. Chronic sleep deprivation for physiologic reasons may cause as much debility as a pathologic disorder. While the definition of sufficient sleep varies, one should generally not work up a complaint of hypersomnolence unless the individual is attempting, on a reasonably regular schedule, to get six to eight hours of sleep per twenty-four hour period. Careful attention must also be paid to alcohol use, since heavy use may disrupt sleep patterns, and may induce or worsen sleep disorders.

In civilian practice, insomnia is the most common sleep complaint. The pattern of disturbance is usually helpful for diagnosis; chronic difficulty initiating sleep is most often associated with anxiety or stress, while early morning awakenings suggest depression. Frequent brief awakenings throughout the night are more suggestive of pathologic sleep disorders, and are a feature of both sleep apnea and narcolepsy.

#### Narcolepsy

Narcolepsy was one of the earliest identified sleep disorders; the first description dating back to 1880. Although it is considered to be a common cause of pathologic hypersomnolence, it is considerably less common than obstructive sleep apnea. The typical age of onset is from late adolescence through the early twenties (because poor sleep hygiene is markedly common in this period of life, and because narcolepsy is permanently disqualifying, it is vital to rule out physiologic sleep disruptions in aviators thought to have narcolepsy). Narcoleptics commonly have a disrupted pattern of sleep, but the hypersomnolence is not simply related to sleep deprivation. Instead, narcolepsy is a neurologic disorder of sleep-state boundaries, characterized by the inability to keep sleep and its manifestations confined to the normal sleeping period. Researchers believe that low

levels of a protein called hypocretin (also known as orexin) may be an underlying cause of narcolepsy. Hypocretin is released by neurons in the lateral hypothalamus. These neurons excite multiple monoaminergic and cholinergic wake-promoting neurons, including histaminergic cells of the tuberomammillary nucleus (TMN). Histamine levels in the CSF of animals were reported to be higher during wakefulness compared with rest. In humans, histaminergic transmission may also fluctuate according to sleep pressure and decrease in the presence of Excessive Daytime sleepiness (EDS). The pathophysiology of decreased histaminergic transmission in patients is unclear. In patients with narcolepsy, lower CSF histamine could reflect the loss of hypocretin neurons, which densely innervate and activate histaminergic neurons in the TMN.<sup>1</sup>

The intrusion of rapid eye movement (REM) patterns into different parts of the sleep-wake cycle may lead to manifestations such as hypnagogic (predormital) and hypnopompic (postdormital) hallucinations, sleep paralysis, and cataplexy, the last characterized by loss of postural control (e.g., head drooping, knees buckling, even falling) associated with strong emotional stimulus (e.g., laughter, anger, surprise). The hypersomnolence of narcolepsy typically manifests as sudden sleepiness requiring a brief nap; after a nap as short as 1-20 minutes, the individual usually awakens feeling refreshed. The combination of hypnogogic hallucinations, sleep paralysis, and cataplexy with excessive daytime sleepiness is classic for narcolepsy, but not all patients will have the complete tetrad. True cataplexy is an important symptom, as it is all but diagnostic for narcolepsy. The diagnosis of narcolepsy without cataplexy is somewhat more challenging. Narcoleptics may also experience episodic lapses of conscious awareness typified by automatic behavior and amnesia. It should be noted that such behavior may also be seen in any individual with sufficient sleep deprivation or certain types of seizures.

If the history suggests narcolepsy and the polysomnogram shows no evidence of an alternative diagnosis, such as sleep apnea, the patient should have 2 weeks of a sleep diary with actigraphy monitoring, followed by overnight polysomnography and a multiple sleep latency test (MSLT) the following day. MSLT measures the amount of time required to fall asleep, and is performed by having the individual lie down in a darkened room and instructed to try to fall asleep. This is repeated three or four more times at two hour intervals, with each trial lasting 20 minutes if sleep does not occur. Normal individuals usually show mean sleep latency (MSL) of at least 8 minutes, with no sleep onset REM periods (SOREMPs) evident during any trial. A MSL less than 8 minutes, with two or more SOREMPs is considered strong evidence of narcolepsy, if a physiologic sleep disorder has been ruled out.

Narcolepsy is usually treated with wake-promoting agents, REM-suppressing medications and prescribed napping periods, but there is no cure for narcolepsy.<sup>2</sup> Neither the disease nor the medications are waiverable for military aviation.

## Obstructive sleep apnea

Obstructive sleep apnea (OSA) is the most common pathologic sleep disorder. Traditional estimates of prevalence suggested that, among American adults ages 30 to 60, 4% of males and 2% of females were affected. However, more recent data suggests that these numbers have increased substantially over the past 2 decades. Data from the Wisconsin Sleep Cohort Study collected from 2007 - 2010 estimated the overall prevalence of OSA in the U.S. for persons age 30 - 70 years of age to be 26%. Prevalence among military aviators is unknown, but because obesity is less common in that population, the rate is likely to be lower. While the prevalence in military aviators

may be lower than the general population, it should be noted that research from the USAF School of Aerospace Medicine's Aeromedical Consultation Service (ACS) has demonstrated an increasing prevalence of both obesity and obstructive sleep apnea in USAF aviators over the last decade. The key to OSA lies in the pattern of muscle activity that occurs in different stages of sleep. The sleep state is associated with a decrease in neuromotor output to pharyngeal muscles. When this occurs against the background of anatomic abnormalities of the upper airway, the pharyngeal airway can become severely narrowed or can close. Numerous factors including edema, obesity, and genetics can alter upper airway anatomy. There are many anatomic risk factors for sleep apnea including macroglossia, lateral peritonsillar narrowing, elongation of the uvula, narrowing of the hard palate, and retrognathia. Factors that reduce upper airway muscle tone (alcohol, sedatives, narcotics, hypnotics) also need to be considered in the evaluation of sleep apnea.<sup>6</sup>

Individuals with OSA are rarely aware of their sleep disorder, even upon arousal. Sleep apnea is usually recognized as a problem by family members who witness the apneic episodes or by a primary care doctor because of the individual's risk factors and symptoms. Most commonly, patients present with vague complaints. Clinical symptoms can include excessive daytime sleepiness (EDS) that usually begins during quiet activities (e.g., reading, watching television), daytime fatigue, feeling tired despite a full night's sleep, morning headaches, personality and mood changes, dry or sore throat, gastroesophageal reflux, and sexual dysfunction. Snoring is a common finding in individuals with OSA. Although not everyone who snores is experiencing sleep apnea, snoring in combination with obesity has been found to be highly predictive of OSA risk. The volume of the snoring is not indicative of the severity of obstruction. However, snoring with witnessed apneas has a 94% specificity for OSA.

In addition to obesity (body-mass index >30), large neck circumference (>17.5 inches) is associated with OSA. In fact, neck circumference is a better predictor of OSA than BMI.<sup>8</sup> Weight gain is often associated with the development or worsening of symptoms. Hypothyroidism may cause or exacerbate OSA, and thyroid stimulating hormone levels should be checked in any patients who exhibit other signs or symptoms of thyroid dysfunction. One should also pay particular attention to drug and alcohol history; heavy alcohol use and sedating medications can cause sleep-disordered breathing that will disappear if the individual is abstains prior to a polysomnogram.<sup>9</sup>

Obstructive sleep apnea (OSA) is a secondary cause of hypertension, with prevalence estimated to be between 38% and 82%. This is double what would be expected in a population of middle-aged Caucasians, even when obesity is accounted for. Despite the high prevalence, evidence of target-organ damage, and increased markers of atherosclerosis, OSA remains largely underdiagnosed and, consequently, undertreated in clinical practice. 13-16

Epidemiologic studies support a causal role of OSA in systemic hypertension, independent of BMI, measures of fat distribution, age, sex, and other possible confounding factors. Randomized, double-blind, placebo controlled trials of patients with hypertension demonstrate that effective treatment of OSA with CPAP lowers blood pressure. A decrease in blood pressure is most pronounced in those with the most severe OSA and who are the most compliant. OSA is a cause of secondary pulmonary hypertension (PH). PH is usually mild, although it can be severe, particularly in the presence of comorbid disorders such as COPD. Treatment of OSA with CPAP may improve PH.<sup>17</sup>

Various neuropsychologic deficits are associated with OSA, mainly in the areas of memory, attention, and executive tasks that require planning, shifting or constructive abilities. Individuals with OSA have decreased ability to initiate new mental processes and to inhibit automatic ones, in conjunction with a tendency for preservative errors. They are also affected with deficits of verbal and visual learning abilities and reduced memory spans. Neurocognitive deficits vary considerably from one individual to another. In the ACS experience, impairment is very rare with mild to moderate OSA, but is more common with severe sleep-disordered breathing. Depressive symptoms are common in OSA, with prevalence as high as 24-45%. 19

In addition to the symptoms and morbidity associated with OSA, there is a growing body of evidence that sleep apnea is associated with an increased risk of mortality. A recently published study from Australia followed a cohort of individuals with OSA over a period of 14 years. The results demonstrated a four-fold increased risk of all-cause mortality in those with moderate to severe OSA.<sup>20</sup>

The STOP-BANG (Snoring, Tiredness during daytime, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, Gender) questionnaire was validated as a screening modality for OSA in the preoperative setting. This instrument is simple questionnaire that consists of 8 yes-or-no questions. Patients were classified as being at high risk for OSA if their STOP-BANG score was 3 or more and were classified as being at low risk if their score was less than 3. This study found that patients at high risk of OSA had a higher risk of pulmonary or cardiac complications, and had an increase length of stay in the hospital. The STOP-BANG questionnaire is concise and easy to administer. It has been validated in surgical patients and has a high sensitivity to identify most patients with OSA, especially moderate and severe OSA.<sup>21</sup>

The Epworth sleepiness scale (ESS) has been universally adopted as an effective screening method to monitor for clinical symptoms of sleep apnea. This questionnaire is used to help determine how likely the patient is to doze off in eight frequently encountered situations (e.g., as a passenger in a car, sitting quietly after lunch, etc.). A 2003 study showed that an ESS score of 12 or greater is considered abnormal and would warrant a more formal evaluation. However, the ESS is still a subjective self-assessment measure and may be inaccurate for a number of reasons. Therefore, if a patient has multiple risk factors for sleep apnea, the individual should be sent for further evaluation if there is a suspicion of sleep apnea despite a low ESS. Excessive daytime somnolence (EDS) is multifactorial in nature and the comorbidities that exacerbate EDS in the setting of OSA are (in decreasing level of importance) depression, BMI, sleep duration (bedtime/wake time) and smoking. Therefore, these items should also be addressed when assessing aeromedical risk and should be included in the waiver submission.

Per the latest American Academy of Sleep Medicine (AASM) Manual for scoring published in April 2016, an apnea must meet both criteria to include drop in peak signal excursion by >90% of pre-event baseline using an oronasal thermal sensor and duration of the drop lasting at least 10 seconds. Hypopnea is defined as a recognizable transient reduction (but not complete cessation) of breathing for at least 10 seconds. This differs from apnea in that there remains some flow of air. In the context of sleep disorders, a hypopnea event is only considered to be clinically significant if it lasts for at least 10 seconds, there is at least a 30% reduction in flow, and it is associated with either an arousal or a 3% or greater desaturation in oxygen saturations. It should be noted that despite the AASM's recommendations, Medicare and many insurance companies only consider hypopneas to

be significant if they are associated with a 4% or greater oxygen desaturation. Apneas and hypopneas can occur multiple times per hour and are both used to calculate the severity of a person's sleep disorder. The Apnea-Hypopnea Index (AHI) is defined as the number of apneas and hypopneas that occur per hour of sleep. This index is used to categorize the severity of sleep. Another measure that is often used is Respiratory Disturbance Index (RDI). Like the AHI, RDI measures respiratory events; however, it also included respiratory effort related arousals (RERAs). RERAs are arousals from sleep that result from reduced airflow, but do not technically meet the definitions of apneas or hypopneas.<sup>8</sup> Because the AASM's most recent guidelines consider reductions in airflow that are associated with a 30% reduction in airflow and an arousal to be a type of hypopnea, most RERAs are now included in the AHI. As a result, the use of RDI in clinical practice has diminished. In general, an individual is considered to have the OSA syndrome if they demonstrate an AHI or RDI of at least 5 events per hour, with the presence of daytime symptoms or an AHI or RDI of 15 or more, independent of symptoms. An AHI or RDI of 5-15 is classified as mild, 15-30 is considered moderate and greater than 30 is considered severe. Additionally, the RDI may also include RERAs that do not meet the definition of a hypopnea (i.e. RERAs that are associated with a reduction in airflow of less than 30%). The ACS and most military treatment facilities use the AASM's recommended definition of AHI (3% desaturation or an arousal) or the RDI, as opposed to Medicare's definition of the AHI (4% desaturation).

Diagnosis of OSA and most pathologic sleep disorders requires polysomnography (PSG). An in sleep lab polysomnography involves monitoring at least one night's sleep with electroencephalography, chin and leg electromyography, electro-oculography, measurements of airflow and thoracic/abdominal excursion, body position and oximetry. Usually continuous electrocardiography and video monitoring are performed as well. While home sleep apnea testing (HSAT) has also been gaining increasing acceptance and has the advantage of convenience and cost, it is not sufficiently sensitive for the purpose of aeromedical disposition. There are four types of sleep monitoring devices. Type 1 monitoring devices are used for technician attended PSGs and are associated with in lab PSG. Type 2 devices record the same variables at Type 1 but are unattended sleep studies. Type 3 devices are the most commonly used HSAT devices and typically measure four to seven physiologic variables including two respiratory variables (respiratory effort and airflow), a cardiac variable (heart rate or electrocardiogram), and arterial oxyhemoglobin saturation via pulse oximetry. The major drawbacks of Type 3 devices include inability to detect arousals, REM sleep vs. NREM sleep vs. wakefulness due to lack of EEG which can then result in inaccurate AHI. For the purposes of a thorough aeromedical evaluation, an in lab polysomnography with Type 1 monitoring devices is therefore required.

As mentioned earlier, polysomnography is the gold standard for the diagnosis of OSA. However, one major problem with sleep laboratories is the huge degree of variability of results. Even accreditation with the American Academy of Sleep Medicine (AASM) is no guarantee, because standards for interpretation have been difficult to establish. Unlike the waiver evaluation, USAF policy does not require that an initial work-up to establish or rule out a sleep disorder in an aviator must occur at a particular site. However, if at all feasible, it is strongly recommended that the initial diagnostic evaluation be arranged at a sleep laboratory in an academic facility (defined as an institution with a sleep fellowship program) to ensure consistency.

The maintenance of wakefulness test (MWT) is a measure of the volitional ability to stay awake. The individual is seated in a quiet, dimly lit room and instructed to remain awake; a total of four 40-

minute trials are conducted at 2-hour intervals. Based on statistical analysis of normative data, a MSL of less than 8 minutes on the 40-minute MWT is abnormal.<sup>22</sup> A MSL of 40 is considered normal, while MSL values between 8 and 40 minutes are considered equivocal. However, it is important to note than in several studies of patients with OSA, performance on driving simulators improved significantly in patients with MSLs greater than 30-34.<sup>23-24</sup> The MWT is not routinely performed during an initial, local evaluation of OSA, but may be employed by the ACS for the purposes of aeromedical disposition.

While multiple treatment options usually exist for sleep apnea, not all are compatible with unrestricted worldwide duty. In the majority of patients, OSA pathology develops as weight increases, the typical history revealing a progression of heroic snoring, observed apneas, and hypersomnolence as mass has progressively increased. Weight loss is the preferred approach in obese patients, with health benefits extending well beyond OSA treatment. The relationship between weight loss and decrease in number of apnea and hypopneas is not linear; 10% weight loss can decrease apneas events by 50%. Flying status can be a powerful motivator for weight loss. However, it should be noted that it is rare for those with moderate or severe sleep apnea to lose enough weight to achieve a normal AHI (less than 5 events per hour). Additionally, even in highly motivated populations, weight loss can be difficult to achieve and maintain. Positional therapy is likely to be helpful when a significant positional component is identified during the sleep study. Medications have largely been ineffective for OSA, and those that have been tried are not approved for flight.

Oral appliances, which attach to the teeth to advance the mandible, are frequently effective in reducing sleep-disordered breathing, are generally well tolerated, and are waiverable without restriction. They are especially effective in those with mild to moderate sleep apnea and in those with a positional component to their disease. Nasal continuous positive airway pressure (CPAP), which acts as a pneumatic stent to maintain airway patency, is usually effective for any degree of sleep apnea and is considered the gold standard treatment. While compliance can be a problem, most of the newer CPAP machines have the ability to record and store usage (compliance) data, making it very easy for practitioners to determine how compliant their patients have been. For active duty personnel, the use of CPAP may restrict worldwide qualification. Current policy only requires I-RILO for moderate, severe, or incompletely treated OSA, and usually results in an assignment limitation code C-1 designation. Regardless of whether or not an IRILO is required, the need for a continuous power supply, clean water and a reasonably dust-free environment to avoid overwhelming the filtering system usually requires theater clearance for CPAP use during deployment.

Several surgical options are available for OSA, including such procedures as uvulopalatopharyngoplasty (UPPP) and maxillary-mandibular advancement (MMA). UPPP is popular, and as a treatment for heroic snoring, it has a high degree of success, at least in the short term. However, for OSA it is only modestly effective, with success in only about 45% of patients, with success defined as a 50% reduction in sleep-disordered breathing, rather than abolition of apneas or control of the clinical manifestations. MMA, a technically more complicated operation, is effective in 90-95% of patients. One of the newest FDA approved treatment modalities for OSA that is not approved for aeromedical use is the hypoglossal nerve stimulation device which is implanted near the collar bone, and is activated remotely. It may be indicated for moderate to

severe OSA patients that have had CPAP failure or intolerance and works by activating the protrusion muscles of the tongue via the hypoglossal nerve to open the lower pharyngeal airway.

## Sleepwalking (Somnambulism)

A sleepwalking episode occurs at least once in 10-30% of children, and 2-3% sleepwalk often. The prevalence of sleepwalking disorder in adults is approximately 4%. Episodes first occur most commonly between 4 to 8 years, with the incidence peaking at age 12, and usually disappear spontaneously by age 15. A family history of sleepwalking is seen in up to 80% of sleepwalking individuals. The risk of sleepwalking increases to up to 60% in children if both parents have a history of sleepwalking disorder. Sleepwalking disorder typically occurs during slow wave stages of non-REM sleep, during the first 1-2 hours of sleep, and is seldom remembered by the individual. During the episode the individual has reduced alertness, unresponsiveness, and a blank stare. They can be quite difficult to arouse during an event. If awakened during a sleepwalking episode the individual is usually confused for several minutes before exhibiting normal wakefulness.<sup>26</sup>

## Central Sleep Apnea

Central sleep apnea is far less common than obstructive sleep apnea. It is characterized by repetitive periods of apnea caused, not from an obstructed airway, but due to a periodic decrease in the central respiratory drive. The diagnosis of central sleep apnea syndrome requires that five or more apneic episodes per hour of sleep be seen on polysomnography. Normal individuals often have occasional central apneas at the onset of sleep, either at the beginning of the sleep period, or after an arousal. These are considered physiologic and only require further investigation if they appear to be causing desaturations or arousals. Another frequently encountered form of central sleep apnea occurs when OSA patients first start to use CPAP therapy. This form of central sleep apnea, known as complex sleep apnea, will usually resolve spontaneously within 6 weeks of starting CPAP therapy. It only requires further work-up and treatment if it persists after 6 weeks. Another common form of central sleep apnea is periodic breathing of altitude. The prevalence increases with altitude. At the altitude of the USAF Academy, nearly one third of patients will demonstrate evidence of central sleep apnea. Other common causes of central apneas include opiate use, congestive heart failure, neurological conditions, and renal dysfunction.<sup>27</sup> Primary or idiopathic central sleep apnea is a rare form of central sleep apnea of unknown cause. Most forms of central sleep apnea typically cause excessive daytime sleepiness, insomnia, or difficulty breathing during sleep.

## Periodic Limb Movements Disorder and Restless Leg Syndrome

Periodic limb movements in sleep are a common finding on polysomnography. They are defined as repetitive limb movements that last between 0.5 and 5 seconds and occur at intervals of 4 to 90 seconds. Periodic limb movements are very common, and there is a debate in the sleep medicine community as to whether the condition should be considered a disorder or a normal physiologic phenomenon. The number of periodic limb movements per hour is referred to as the periodic limb movement index (PLMI). The number of times per hour that one of these movements causes an arousal is called the periodic limb movement arousal index (PLMAI). Periodic limb movement disorder is defined as a PLMI greater than 15 events per hour. Generally speaking treatment is only indicated if the condition is symptomatic or if the PLMAI is greater than 5 events per hour.

In contrast to periodic limb movement disorder, restless leg syndrome (RLS), is a clinical diagnosis. It is characterized by an uncomfortable sensation in the legs (i.e. pain, cramping, creeping/crawling sensation) that is worse just before bed, is accompanied by a strong urge to move or stretch, improves with movement, and then quickly returns afterward.

Both periodic limb movement disorder and RLS are often idiopathic, though they have been associated with low ferritin levels. It is recommended that ferritin levels be checked and iron supplementation be initiated for ferritin levels below 50 mcg/L. Elimination of alcohol, tobacco, and caffeine can have positive effects. Pharmacotherapy is available, but should only be initiated if the individual is symptomatic. Medications for the treatment of periodic limb movement disorder and RLS are not waiverable due to significant side effect profiles.

#### IV. Aeromedical Concerns.

With the exception of somnambulism, any of the sleep disorders above may result in excessive daytime sleepiness and an inability to maintain the alertness necessary for safety while flying. Cognitive function and neuromuscular coordination may both be affected by the sleep disorder and/or the treatment modalities used. When called upon to perform in operational situations with less than optimal sleep, those with OSA are already sleep deprived. Furthermore, when faced with sleep deprivation, normal individuals typically respond by altering sleep patterns, e.g., longer periods of REM sleep. This is likely a physiologic response and serves to increase sleep efficiency in normal individuals. However, OSA tends to be most severe in REM. The result is that individuals with OSA may have more than the usual difficulty in adjusting to sleep deprivation or the circadian rhythm disruption which occurs with travel across time zones. This would present an additional hazard to a flyer who may deploy several time zones away and would still be expected to perform flying duties.

If an aviator is diagnosed with OSA, they should be made DNIF, and treatment should be initiated as soon as possible. All aviators who are obese or overweight should be treated with weight loss. Most patients will also require treatment with an adjunctive therapy such as an oral appliance, positional therapy, or CPAP. After weight loss is achieved, the adjunctive therapy should only be discontinued if the patient has demonstrated a normal AHI (less than 5 events per hour) on PSG and resolution of symptoms off of therapy. Surgery may also be considered as an adjunctive therapy, though given the morbidity and variable efficacy, it is difficult to recommend surgery as a first-line therapy. If the aviator does not have symptoms clearly associated with the diagnosis, the ACS recommends that the disorder be confirmed at an academic sleep center such as Wilford Hall Ambulatory Surgical Center, Walter Reed National Military Medical Center or the 88<sup>th</sup> Medical Group at Wright-Patterson AFB before considering a surgical procedure. The neurocognitive deficits associated with OSA can, for the most part, be mitigated with treatment, such as CPAP therapy. However, it is important to note that in one study of patients with sleep apnea and neurocognitive deficits, nearly all the improvement seen with CPAP use was lost after just one night without therapy. The patients with sleep apnea and neurocognitive deficits, nearly all the improvement seen with CPAP use was lost after just one night without therapy.

If narcolepsy is diagnosed by an outside sleep laboratory, the aviator should be referred to the ACS for confirmation of the diagnosis. Although this diagnosis, if confirmed, will result in permanent disqualification, the ACS has seen multiple instances of aviators who were improperly diagnosed as narcoleptic.

Lastly, individuals with history of somnambulism can injure themselves during sleepwalking episodes as complex and also inappropriate behaviors can occur, including driving, going outside, and even walking out of windows. Therefore, those with somnambulism in a combat environment are considered to be a hazard to themselves and to others.

| ICD 9 codes for sleep disorders |   |  |
|---------------------------------|---|--|
| 307.4                           | Specific disorders of sleep of non-organic origin |  |
|                                 | (including Sleepwalking)                          |  |
| 327.42                          | Primary insomnia                                  |  |
| 347                             | Narcolepsy (with or without cataplexy)            |  |
| 780.57                          | Unspecified sleep apnea                           |  |
| 327.51                          | Periodic limb movement disorder                   |  |
| 333.94                          | Restless leg syndrome                             |  |

| ICD 10 codes for sleep disorders |  |  |
|----------------------------------|--|--|
| F51.9                            | Sleep disorder not due to a substance or known |  |
|                                  | physiologic condition, unspecified             |  |
| G47.52                           | REM sleep behavior disorder                    |  |
| G47.411                          | Narcolepsy (with cataplexy)                    |  |
| G47.419                          | Narcolepsy (without cataplexy)                 |  |
| G47.30                           | Sleep apnea, unspecified                       |  |
| G25.8                            | Restless leg syndrome                          |  |

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## WAIVER GUIDE

Updated: Jul 2014

Supersedes Waiver Guide of Apr 2010

By: Maj John E. Miles (RAM XV) and Dr. Dan Van Syoc Reviewed by Dr. Terry Correll, ACS staff psychiatrist

## **CONDITION:**

Somatic Symptoms and Related Disorders (Jul 2014)

## I. Waiver Consideration.

Somatic symptom disorders including, but not limited to illness anxiety disorder or conversion disorder are disqualifying for all classes of flying in the US Air Force. Consideration for a waiver will only be entertained if the aviator is successfully treated and remains off all psychotropic medication for 12 months. Factitious disorders are disqualifying for all flying classes to include retention on active duty; however, for retention, factitious disorders are handled administratively as unsuiting conditions in accordance with DoDI 1332.38 E5.1.3.9.7. 12, 13

Malingering is not considered a mental illness. In DSM-5, malingering receives a V-code as one of several presenting problems that may become a focus of clinical attention or that may exacerbate or otherwise affect the diagnosis, course, prognosis, or treatment of a patient's mental disorder.<sup>1</sup> As such, it too is considered unsuiting rather than unfitting for continued military service and any patient exhibiting such behavior should be referred to the chain of command. As specified in Article 115 of the Uniformed Code of Military Justice (UCMJ), any person who for the purpose of avoiding work, duty, or service feigns illness, physical disablement, mental lapse or derangement; or intentionally inflicts self-injury; shall be punished as a court-martial may direct.<sup>14</sup>

Thus, before submitting a case for waiver consideration, the base-level flight surgeon must first discern whether the condition is unsuiting vs. unfitting for service. If the Airman requires a fit/unfit determination, the case needs MEB action; if the airman requires a suited/unsuited determination, the case needs consideration of an administrative separation or discharge via the chain of command.

Table 1: Waiver potential for Somatic Symptoms and Related Disorders

| Flying Class (FC) | Condition            | Waiver Potential <sup>1</sup> Waiver Authority |
|-------------------|----------------------|--|
| I/IA              | Somatic Symptoms and | No   |
|                   | Related Disorders    | AETC   |
| II/III and        | Somatic Symptoms and | Yes <sup>2</sup>                               |
| ATC/GBO/SWA       | Related Disorders    | MAJCOM   |

<sup>1</sup> No indefinite waivers.

AIMWTS search in Apr 2014 revealed 23 cases; 4 had the diagnosis of conversion disorder, 1 had the diagnosis of pain disorder, 1 had the diagnosis of hypochondriasis, 7 had the diagnosis of somatization disorder, and 10 had the diagnosis of undifferentiated somatoform disorder. Breakdown of the cases revealed: 0 FC I/IA cases, 9 FC II cases (5 disqualified), 8 FC III cases (5 disqualified), 2 MOD cases (2 disqualified), 4 ATC/GBC cases (3 disqualified).

<sup>2</sup> For all UNTRAINED individuals (FC I/IA, FC II/III, and ATC/GBO/SWA), a waiver is NOT considered.

# II. Information Required for Waiver Submission.

Submitting a Mental Health Waiver Guide:

AFI 48-123 –MSD, 6 FEB 2014, Q1 and the Aeromedical Consultation Service (ACS) Waiver Guide addresses waiver evaluations

| C/ 1   | -    | 41  | • 4     |       | e   | •      |            | Ω  |
|--------|------|-----|---------|-------|-----|--------|------------|----|
| Step 1 | - IS | the | aviator | readv | tor | waiver | submission | a? |

| n      | Waiver is submitted when 1) the member is asymptomatic and 2) medications/psychotherapy treatment have been completed, as applicable to diagnostic   |
|--------|--|
| S      | category, for the specified time-frame below (Note: psychotherapy "booster sessions", and sometimes antidepressants, are permissible and often advisable after initial symptom resolution):              |
|        | 1 Year—Psychotic Disorders & Somatic Symptom and Related Disorders   |
|        | 6 Months—Mood Disorders, Anxiety Disorders & Suicidal Behavior   |
|        | Discretion of Flight Surgeon—Adjustment Disorders & "Other Conditions" (V-Codes) requiring waiver  |
|        | For Traumatic Brain Injury cases, please refer to TBI Waiver Guide   |
|        | For aviators with any other psychiatric disorders, please refer to AFI 48-123 and ACS Waiver Guide   |
|        | To be considered for an aeromedical waiver, any disqualifying condition must meet the following criteria per AFI 48-123 Section 6B, 6.2.1.1 through 6.2.1.6. (pg.31):                                    |
|        | Not pose a risk of sudden incapacitation   |
|        | Pose minimal potential for subtle performance decrement, particularly with regard to the   |
|        | higher senses Be resolved, or be stable, and be expected to remain so under the stresses of the aviation environment   |
|        | If the possibility of progression or recurrence exists, the first symptoms or signs must be easily detectable and not pose a risk to the individual or the safety of others                              |
|        | Cannot require exotic tests, regular invasive procedures, or frequent absences to monitor for stability or progression   |
|        | Must be compatible with the performance of sustained flying operations   |
| Mental | Before beginning the Aeromedical Summary (AMS), Flight Surgeon must obtain Health consultation and ensure it contains items specified below: tions for the Mental Health Provider                        |
|        | ntal health evaluation must include a <b>comprehensive written report</b> addressing:  |
|        | Consultation must address each criteria in Step 1B   |
|        | Clinical mental health history (description of symptoms, treatment modality, frequency and compliance with treatment, relevant personal and family history, and perceived impact on occupational duties) |
|        | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)  |

|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)  ** for alcohol cases, please comment on carbohydrate-deficient transferrin (CDT) results**   |
|----------|---|
|          | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, input from line leadership, if possible, and please address current state of any triggers for the mental illness)   |
|          | Current and past aviation related duties and any history of current and past occupational performance difficulties (to include perceived impact of mental health condition on performance   |
|          | of duties) Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)  |
|          | Summary and interpretation of psychological/neuropsychological testing results (recommend MMPI-2, NEO PI-R, or similar personality test). For neuropsychological cases, please contact ACS neuropsychologist (Dr. Gary Ford, DSN: 798-2704) for guidance on recommended neuropsychological tests.  Current mental status                      |
|          | Diagnosis   |
|          | Motivation to fly or engage in special duty operations (past and current)   |
|          | Recommendation for future psychological and medical treatment   |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
|          | Copies of all records (mental health/ADAPT/inpatient) and raw testing data should be on hand for shipment to ACS Neuropsychiatry Branch   |
| Step 3 - | Items for the Flight Surgeon to include in the AMS:  AMS must clearly address each criteria in Step 1B and the risk to the member, mission, and safety  |
|          | Summarize Mental Health history and focus on occupational impact  ** If 2 or more months have passed since the comprehensive evaluation/report was completed, the flight surgeon should address how the member has done since and consult with the mental health provider if the member has been seen at mental health since the evaluation** |
|          | Medication history (dates of initial prescription and termination, reason for termination, dosage, compliance, response, clinical course since termination)   |
|          | Laboratory results (i.e., thyroid, liver function tests, drug screen, CDT, CBC, chemical profile)  ** for alcohol cases, please comment on carbohydrate-deficient transferrin (CDT) results**   |
|          | Current psychosocial situation (marital and occupational, interview with spouse/supervisor, if possible - please address current state of any triggers for the mental illness)  |
|          | Habits (exercise, diet, medications, supplements, alcohol, tobacco, caffeine, energy drinks, sleep)   |
|          | Current mental status   |
|          | Diagnosis   |
|          | Motivation to fly (past and current)  |
|          | Recommendation for future psychological and medical treatment   |
|          | Prognosis (estimate of symptom recurrence, potential impact on future aviation related duties)  |
| Step 4 - | Letter of support from command  |
|          |   |

| Comprehensive mental health written-report  |
|---|
| Confirm mental health has made copies of chart(s) and testing. When requested send to:  |
| ACS Aerospace Medicine Branch, USAFSAM/FECA<br>c/o Neuropsychiatry Branch<br>2510 Fifth Street Bldg 840<br>Wright Patterson AFB, OH 45433-7913<br>Fax: (937) 904-6296 DSN: 674-9296 |

Please feel free to contact the ACS Neuropsychiatry Branch with questions: SSgt Krista Traut 798-2653, or Mr. John Heaton: 798-2766

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for somatic symptom and related disorders should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of the disorder and all treatments administered, the current status of any social, occupational, administrative or legal problems associated with the case, and an analysis of the aeromedical implications of this particular case history.
- C. Consultation from a psychiatrist or psychologist. All treatment notes from the treating mental health professional as well as an MEB-type narrative summary of the mental health record are required.
- D. Report of all psychological testing, if performed.
- E. Letter of support from the aviator's supervisor.

The AMS for <u>waiver renewal</u> should include the following:

- A. Interval history
- B. Treatment current therapy for the condition, if any.
- C. Consultation from psychiatry/psychology if accomplished since the last waiver request.

# III. Overview.

Five diagnoses are grouped within the category of somatic symptom and related disorders: somatic symptom disorder, illness anxiety disorder, conversion disorder, psychological factors affecting other medical conditions, and factitious disorder. These conditions were previously classified in the Fourth Edition of the Diagnostic and Statistical Manual of Mental Health Disorders (DSM-IV) as either somatoform disorders (somatization disorder, conversion disorder, pain disorder, hypochondriasis, body dysmorphic disorder, undifferentiated somatoform disorder, and somatoform disorder NOS) or factitious disorders. With the publication of DSM-5 in May 2013, the conditions were reclassified in an effort to simplify diagnosis in the primary care setting by focusing on the conditions' distressing somatic symptoms and the accompanying abnormal thoughts, feelings, and behaviors. The new classification removed the requirement that the somatic symptoms be medically unexplained. Although often similar to these disorders in presentation, malingering is not

considered a mental illness even when it impacts the diagnosis, prognosis, or treatment of a medical condition.

The following discussion will focus on somatic symptom disorder, conversion disorder, and factitious disorder. In general, these conditions are more common among females, ethnic minorities, those with fewer years of education, and those of lower socioeconomic status. The 12-month prevalence rate for any somatic symptom or related disorder is about 6 percent of the general population. In women, these disorders have been associated with childhood sexual abuse and recent exposure to physical or sexual violence. These conditions are also strongly associated with other psychiatric disorders, especially anxiety and depression.<sup>2</sup>

Somatic symptom disorder is a new diagnosis which includes many conditions previously classified as somatization disorders or hypochondriasis. Diagnosis requires the persistence of one or more somatic symptoms that are very distressing or significantly interfere with normal functioning. The condition is marked by excessive thoughts, feelings, or behaviors regarding the symptoms. The symptoms may or may not be medically explained.<sup>1</sup>

Conversion disorders are characterized by neurologic symptoms (e.g. weakness, paralysis, seizures, blindness) that are incompatible with recognized neurologic or medical conditions but still cause distress and/or psychosocial impairment.<sup>1</sup> Diagnosis depends upon clinical findings that reveal a symptom to be incongruent with anatomy, physiology, or known diseases, or inconsistent at different times.<sup>2</sup> Conversion disorders seldom occur for the first time after the age of 35, and symptoms are markedly more common among women than men. In fact, the disorder was originally known as hysteria, a name derived from the Greek word for uterus (□□□□□) because of the ancients' belief that the symptoms arose from a physical displacement of this organ. Studies have found that over a quarter of normal post-partum and medically ill women report having had conversion symptoms at some point during their lives. Although the prognosis for conversion disorder is initially good with symptoms frequently resolving relatively quickly, up to 25% of patients relapse within one year. Cases with an acute onset, a clearly identifiable provoking stressor, and a short interval between onset and treatment tend to do best. Cases manifesting as blindness, aphonia, or paralysis tend to do better than those involving seizures or tremors.<sup>3</sup>

In both somatic symptom disorder and conversion disorder, symptoms are not seen as intentional, voluntary, or consciously produced.<sup>2</sup> In factitious disorders and malingering, on the other hand, an individual intentionally produces or feigns physical or psychological symptoms, presenting himself or herself to others as ill, impaired, or injured. In factitious disorders, the deceptive behavior is evident even in the absence of obvious external rewards. The factitious disorder patient's primary goals are to assume the sick role and to receive medical, surgical, or psychiatric care (i.e., to feel "cared for"). In malingering, symptoms are consciously produced or feigned because of a clear external incentive, e.g., to avoid an undesirable deployment, to be discharged from the military, or to obtain monetary compensation.<sup>2</sup>

Factitious disorder may be suspected when a patient presents with a dramatic but inconsistent medical history. Symptoms may be unclear and changing and may become more severe after treatment has begun. New symptoms may appear following negative lab results and predictable relapses may follow improvements. The patient may display extensive knowledge of hospitals and medical jargon, as well as a textbook presentation of his or her illness. The patient may display an

unusual willingness or eagerness to undergo medical tests, operations, or other procedures and may have a history of seeking treatment from multiple providers. The patient may be reluctant to allow health care professionals to talk to family members, friends, and previous providers. A particularly severe and chronic form of factitious disorder is Münchausen syndrome which is marked by the following three components: recurrent hospitalizations, travel from hospital to hospital (peregrination), and pathological lying (pseudologia fantastica). While the majority of cases of factitious disorder involve physical symptoms, some patients primarily feign psychological symptoms. Psychological complaints (like physical ones) encompass a broad spectrum of symptoms, including depression, anxiety, psychosis, bereavement, dissociation, posttraumatic stress, and even homicidal ideation.<sup>5-7</sup>

There are two significant negative consequences to somatic symptom and related disorders. First is the excess health care cost resulting from frequent medical visits, diagnostic testing, invasive procedures, and hospitalizations. Second is the adverse impact on the doctor-patient relationship that is common in this setting. Management of these disorders frequently requires that patients spend an extended time away from their duties. Even when present for duty, patients are often preoccupied with their physical symptoms and less devoted to mission-oriented tasks. Their symptoms may lead to medical recommendations for multiple duty limiting restrictions.

Among aviators, somatic symptom and related disorders may represent a difficult manifestation of fear of flying. As detailed in DeHart's Fundamentals of Aerospace Medicine, chronic physical or physiologic symptoms may be presented by a flier (sometimes preceded by the words, "I'd like to fly, but...") as incompatible with continuing to fly. This attitude presents a striking contrast to that of most fliers who insist on flying in spite of their symptoms. A reluctant flier's symptoms can arise from an unconscious conflict between anxiety about flying and a greater anxiety about giving up the role of the aviator. "Involuntary" grounding for physical reasons beyond the flier's conscious control offers an acceptable way out of the conflict. As an example, with an unconscious conflict presenting as a conversion disorder, the aviator has no conscious anxiety about flying, and therefore responds to any question concerning apprehension in flight with denial because the question represents a challenge to their defense that the symptoms offer against the intolerable but unconscious underlying anxiety. The flier may have little concern about any disease the symptoms represent, concentrating instead on being removed from flying duties in order to avoid the distress. The entire presentation of the case differs from that of the usual aviator who does not want to be grounded. Three clinical observations may help identify the unconscious aspect of the conversion symptoms. First, the flier tends to describe the symptoms in terms of their effect on flying. Second, the flier may express no particular anxiety about being significantly ill, and have little interest in specific treatment. Third, if asked, "Will you go back to flying when you are well?" the flier may equivocate or signal reluctance. Identifying the somatoform nature of the problem may allow the physician to avoid unnecessary, expensive, or invasive diagnostic procedures. Even if the psychologic nature of the problem is established, the flier is unlikely to agree with the formulation and to cooperate in necessary psychotherapy. The nature of the symptoms (headaches, various pains, sensory deficits, autonomic disturbances of the gastrointestinal tract) may preclude safe return to flying duties.<sup>9</sup> All the somatic symptom and related disorders may be a defense against fear of flying so it is important to evaluate for recent stressors surrounding flying duty in any of the somatoform presentations.

There is no specific therapy for somatic symptom and related disorders. Management of these conditions requires a good clinician-patient relationship. Attempts should be made to limit a patient's routine care to a single primary clinician and hospital, although in all aeromedical cases, care should also be closely coordinated with psychiatric consultation. Cognitive Behavioral Therapy (CBT) has been found to be an effective treatment for these disorders in some settings. Any underlying medical illnesses must be fully treated while also protecting patients from self-harm and harmful medical procedures. Excessive, repetitive, and unnecessary diagnostic testing should be avoided, especially invasive medical and surgical workups. The doctor needs to be supportive, yet realistic in his or her treatment course. Once firmly established, somatic presentations of fear of flying may be quite resistant to therapy. <sup>2, 6, 9, 10</sup>

## IV. Aeromedical Concerns.

These disorders have a chronic course with patients making repeated visits to physicians due to multiple physical or somatic complaints. The attendant somatic concerns and behaviors interfere with flying availability and reliability. Because of the chronic and recurrent nature of these disorders, treatment offers only a weak hope of returning to flying status; motivation to fly, or lack thereof, significantly influences the aviator's prognosis. These individuals are frequently not motivated for psychotherapy, and may attempt to change physicians when confronted. Therefore, consider conservative medical management and reassurance after ruling out possible organic causes for complaints.

| ICD-9 codes for somatic symptom and related disorders |   |  |  |
|---|---|--|--|
| 300.11  | Conversion disorder                                   |  |  |
| 300.7   | Hypochondriasis                                       |  |  |
| 300.81  | 300.81 Somatization disorder                          |  |  |
| 300.82  | Undifferentiated somatoform disorder                  |  |  |
| 300.16  | Factitious disorder with predominantly psychological  |  |  |
|   | signs and symptoms                                    |  |  |
| 300.19  | 300.19 Other and unspecified factitious illness       |  |  |
| 301.51  | Chronic factitious illness with physical symptoms     |  |  |
| 307.89  | Other pain disorders related to psychological factors |  |  |
| V65.2   | Person feigning illness                               |  |  |

| ICD-10 codes for somatic symptom and related disorders |   |  |
|--|---|--|
| F44.4  | Conversion disorder with motor symptoms or deficit        |  |
| F44.6  | Conversion disorder with sensory symptoms or deficit      |  |
| F45.21   | Hypochondriasis   |  |
| F45.0  | Somatization disorder                                     |  |
| F45.1  | Undifferentiated somatoform disorder                      |  |
| F68.11   | Factitious disorder with predominantly psychological      |  |
|  | signs and symptoms  |  |
| F68.8  | Other specified disorders of adult personality behavior   |  |
| F68.12   | Factitious disorder with predominantly physical signs and |  |
|  | symptoms  |  |
| F45.42   | Pain disorder with related psychological factors          |  |
| Z76.5  | Malingerer (conscious simulation)                         |  |

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- 11. AFI 48-123, 5 Nov 2013.
- 12. DoD Instruction 1332.38, 14 Nov 1996.
- 13. Medical Standards Directory (MSD), 6 FEB 2014.
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## Spinal Curvature, Abnormal (Kyphosis, Scoliosis, and Lordosis) (Sep 2019)

Reviewed: Lt Col David Navel (RAM 20), Maj Andrew Long (RAM 20), Dr. Van Syoc (ACS Waiver Guide coordinator), Col Brandon Horne (AF/SG orthopedic surgery consultant), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

## **Significant Changes:**

The overview and aeromedical concerns were shortened and condensed into one section. Table 1 was reformatted to be more succinct. The AIMWTS review was updated for the last 5 years.

## I. Waiver Consideration

For FC I/IA, FC II, FC III, and SWA, lumbar scoliosis (LS) >20° or thoracic scoliosis (TS) >25° by Cobb method, any abnormal curvature producing pain, interference with function, or noticeable deformity when dressed, or abnormal curvature which is progressive are disqualifying IAW the MSD K11. Further, according to K10 of this MSD, LS >30°, TS >30°, kyphosis or lordosis (K/L) >55° K/L or any spinal deviation interfering with function, vocation or wear of the military uniform or equipment is disqualifying for retention as well as all flying and special operator duties. Table 1 explains the aeromedical waiver potential for all flying classes.

Table 1: Waiver potential for flying class and degree of scoliosis kyphosis and lordosis

| Flying Class (FC) | Condition   | Waiver Potential<br>Waiver Authority |
|-------------------|---|--------------------------------------|
| FC I/IA           | Lumbar Scoliosis (LS): >20° or<br>Thoracic Scoliosis (TS): >25° or<br>Kyphosis/Lordosis (K/L): >55° or  | No<br>AETC                           |
|                   | Any abnormal curvature producing noticeable deformity when dressed, pain, interference with function, or which is progressive.  | No<br>AETC                           |
| FC II/III<br>SWA  | Asymptomatic LS: 20-30° or<br>Asymptomatic TS: 25-45°   | Yes <sup>1</sup><br>MAJCOM           |
|                   | Asymptomatic LS: ≥30° or<br>Asymptomatic TS: ≥45° or<br>Asymptomatic K/L: ≥55°  | Yes, IIB <sup>1</sup><br>AFMRA       |
|                   | Any abnormal curvature producing noticeable deformity when dressed, pain, interference with function, or which is progressive.  | No <sup>2</sup><br>MAJCOM            |
| ATC, GBO,<br>SWA  | Lumbar or Thoracic Scoliosis ≥ 30°<br>Kyphosis/Lordosis (K/L): >55°<br>Any abnormal curvature producing noticeable<br>deformity when dressed, pain, interference with<br>function, or which is progressive. | Yes<br>MAJCOM                        |

<sup>1.</sup> No waiver for untrained FC II and FC III.

## **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and any treatment.
  - a. History when deformity first noticed, who discovered, symptoms, treatment.
  - b. Physical document gait, range of motion, motor and sensory testing of lower extremities, including reflexes.
- 2. X-ray results of the spine by the Cobb Method.
- 3. Orthopedic consult, including any follow up notes.
- 4. Document full physical activity, or include any specific activity limitations.
- 5. FL4 with RTD and ALC status, if member did not meet retention standards.
- 6. Any other pertinent information.

<sup>2.</sup> If MEB required, waiver authority is AFMRA for FC II.

7. The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

## B. Renewal Waiver Request:

- 1 Summary noting any interval change.
  - a. History symptoms and activity level.
  - b. Physical document gait, range of motion, motor and sensory testing of lower extremities, including reflexes.
- 2 X-ray results if symptoms develop (back pain, neurologic, etc.).
- 3 Orthopedic consult if there are symptoms or evidence of progression.
- 4 Any other pertinent info.
- 5 The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

### **III. Aeromedical Concerns**

Abnormal spinal curvature includes excessive scoliosis, kyphosis, and lordosis. Although scoliosis is defined as a Cobb angle  $>10^{\circ}$ , progression is likely in adolescents with Cobb angles  $>20^{\circ}$ . In those who have stopped growing, scoliosis  $<30^{\circ}$  is considered stable but scoliosis  $>30^{\circ}$  may be expected to progress  $1^{\circ}$  per year. Treatments may include physical therapy, bracing or surgery. Orthopedic referral is typically indicated when back pain is refractive to conservative therapy, when there is any neurological abnormality, or when the Cobb angle is:

- 1)  $>20^{\circ}$  for the lumbar curve, or
- 2)  $>25^{\circ}$  for the thoracic curve, or
- 3) >55° for thoracic kyphosis or lordosis.

Primary aeromedical concerns involve the increased risk of fracture or other spinal injuries. Additional risks of sudden incapacitation, critically distracting symptoms, or functional limitations during flight may accompany clinically significant or progressive spinal curvatures.

Abnormal spine curvature increases risk of spine fracture during high-G exposures, particularly with ejection seat use or hard landings in rotary wing aircraft. Vertebral fractures frequently occur at loads exceeding the set ejection seat exposure limit of 20G but can occur with forces as low as 10-12Gs when the spine is not vertical. The upper body center of gravity is anterior to the spine and kyphoscoliosis shifts the center of gravity further forward out of vertical alignment. This deviation increases the risk for flexion compression fractures.

Review of AIMWTS in Jun 2019 for the previous 5 years revealed 49 submitted waivers for abnormal spinal curvature. Breakdown of the cases revealed: 8 FC I/IA cases (5 disqualified), 11 FC II waivers (0 disqualified), 7 RPA waivers, 20 FC III cases (7/20 disqualified, 1 with significant pain and 1 with concurrent disqualifying conditions), and 1 GBC case (1/1 disqualified with a concurrent disqualifying condition).

| ICD-9 codes for | ICD-9 codes for Disease/Condition          |  |  |
|-----------------|--|--|--|
| 737.20          | Lordosis (acquired) postural               |  |  |
| 737.29          | Other Lordosis acquired                    |  |  |
| 737.30          | Scoliosis (& Kyphoscoliosis)               |  |  |
| 737.34          | Thoracogenic scoliosis                     |  |  |
| 737.39          | Other Kyphoscoliosis & scoliosis           |  |  |
| 737.42          | Lordosis associated with other conditions  |  |  |
| 737.43          | Scoliosis associated with other conditions |  |  |

| ICD-10 codes f | ICD-10 codes for Disease/Condition          |  |  |
|----------------|---|--|--|
| M40.40         | Postural lordosis, site unspecified         |  |  |
| M40.50         | Lordosis, unspecified, site unspecified     |  |  |
| M41.9          | Scoliosis, unspecified                      |  |  |
| M41.30         | Thoracogenic scoliosis, site unspecified    |  |  |
| M41.80         | Other forms of scoliosis, site unspecified  |  |  |
| M41.50         | Other secondary scoliosis, site unspecified |  |  |

# **IV. Suggested Readings**

- 1. Negrini S, Donzelli S, Aulisa AG, et al. 2016 SOSORT guidelines: orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth. Scoliosis and Spinal Disorders, 2018; 13(3).
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# **Spinal Fracture Mar (2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

## **Significant Changes:**

**Updated Waiver Considerations and References** 

#### I. Waiver Consideration

Fractures or dislocations of the vertebrae are disqualifying for US Air Force FC I, II and III aircrew, as well as for SWA airmen. Fractures or dislocations of the vertebrae are not disqualifying for ATC or GBO personnel. Transverse or spinous process fractures are not disqualifying if asymptomatic following recovery. Ejection/high Gz waiver limitation recommendations are based on severity of fracture, time since injury, treatment, and functional status of the aviator. For compression fractures with vertebral body height loss less than or equal to 25%, an unrestricted waiver recommendation is possible. For vertebral body fractures with greater than 25% compression, pilots and navigators may be considered for categorical FC IIB waiver, but FC I/IA applicants will typically not be considered for a waiver. If, after adequate healing time, there are residua such as chronic pain, decreased mobility, neurological injury, or other medical disease, aeromedical disqualification may be appropriate. Surgically-treated compression fractures normally heal well and are usually recommended for categorical waiver. Traumatic thoracolumbar compression fractures treated with vertebroplasty (VP) or balloon kyphoplasty (BKP) may be considered for unrestricted waiver after six months. VP is injection of bone cement into a vertebral body and BKP is placement of a balloon into the vertebral body, followed by an inflation/deflation sequence to create a cavity prior to cement injection. These procedures primarily address neurologic instability-related pain symptoms and do not affect mechanical stability. The use of a biologic-based cement agent is recommended, as this does allow the potential for new bone deposition.

Burst fractures managed nonoperatively can be aeromedically managed as a compression fracture for waiver consideration. Waived burst fracture aviators should have annual radiographs with interim evaluation to ensure no progression of kyphosis, until they are demonstrated to be stable. Spinous process fractures are commonly seen with direct trauma involving sudden deceleration and forced flexion, and tend to be stable. Parachutists who have fully healed from an uncomplicated and non-surgical spinal fracture should have at least one year post-injury/surgery observation and recovery before waiver consideration.

For cases of spinal fracture with an associated herniated nucleus pulposus, please consult the Waiver Guide chapter on Herniated Nucleus Pulposus and Spinal Fusion, and apply the more restrictive waiver criteria.

Table 1: Waiver potential for spinal fracture

| Flying Class (FC) | Waiver Potential   | Waiver Authority | ACS Review or Evaluation |
|-------------------|--------------------|------------------|--------------------------|
| FC I/IA           | No                 | AETC             | No                       |
| FC II             | Yes <sup>1</sup>   | AFMRA            | Yes                      |
| FC III            | Yes <sup>1</sup>   | MAJCOM           | At MAJCOM Request        |
| Parachute         | Yes <sup>1,2</sup> | MAJCOM           | At MAJCOM Request        |
| SWA               | Yes <sup>1,2</sup> | MAJCOM           | At MAJCOM Request        |

- 1. Compression fractures with >25% vertebral body height loss are usually recommended for restricted waiver.
- 2. Spinal fractures treated with hardware in parachutists are generally disqualifying for continued parachute duties.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

# A. Initial Waiver Request:

# Waiver Request:

- 1. Minimum observation times before aeromedical waiver consideration:
  - a. Compression fractures:
    - 3 months for FC II/FC III managed conservatively
    - 6 months for FC II/FC III if treated with BKP or VP
    - 1 year for parachute duties
  - b. Burst fractures:
    - 6 months for FC II/FC III
    - 1 year for parachute duties
  - 2. History of injury, immediate exam results, and treatment.
  - 3. Reports of consultations, diagnostic testing, imaging, procedures or operations as applicable, and images from initial and current radiographic studies.
  - 4. Reports and images from current dynamic (flexion-extension) radiographs and also, if applicable, current MRI or CT studies. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
  - 5. Consultant note clearing the aviator for return to duty, listing any specific activity limitations.
  - 6. Current spinal and neurologic examination findings.
  - 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.

- 3 Current spinal and neurologic examination findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## **III. Aeromedical Concerns**

Aeromedical concerns include the effects of any residual neurologic or cognitive symptoms on operational safety and mission effectiveness, future risk of new symptom development, and future risk of recurrence. Even after healing, ejection or high Gz load stressors may predispose to repeat fracture and, more ominously, spinal cord damage. Limited mobility after cervical fracture healing, fusion, or fixation can limit scanning from the cockpit and performance under Gz loading with neck rotation. Thoracolumbar fractures can also limit mobility or distract due to pain, but are generally not as limiting for aviation duties. A fully healed uncomplicated spinal fracture should tolerate the traumatic forces from military parachuting.

Review of AIMWTS through Jan 2019 revealed a total of 364 cases submitted with a diagnosis of spinal fracture. Of this total, 45 were FC I/IA (14 disqualified), 150 were FC II (14 disqualified), 6 were RPA pilots (0 disqualified), 151 were FC III (31 disqualified), 10 were ATC/GBC (3 disqualified), and 2 were MOD (0 disqualified).

| ICD-9 Codes for Spinal Fractures |   |
|----------------------------------|---|
| 805                              | Fracture of vertebra without mention of cord injury |
| 806                              | Fracture of vertebra with spinal cord injury        |

| ICD-10 Codes for Spinal Fractures |                               |
|-----------------------------------|-------------------------------|
| S12.0 - S12.9                     | Fracture cervical vertebra    |
| S22.0                             | Fracture of thoracic vertebra |
| S32                               | Fracture of the lumbar spine  |

# **IV. Suggested Readings**

- 1. Kaji A. Evaluation and acute management of cervical spinal column injuries in adults. UpToDate, Oct 0, 2019.
- 2. Kaji A, Hockberger RS. Spinal column injuries in adults: definition, mechanisms and radiographs.\_UpToDate, Apr 11, 2018
- 3. Kaji A, Hockberger RS. Evaluation of thoracic and lumbar spinal column injury. UpToDate, Aug 30, 2018.
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- 5. Wood KB, Li W, Lebl DR, and Ploumis A. Management of thoracolumbar spine fractures. Spine J, 2014; 14: 145-64.

- 6. McBratney CM, Rush S, and Kharod CU. Pilot Ejection, Parachute, and Helicopter Crash Injuries. J Spec Oper Med 2014; 14:92-94.
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### WAIVER GUIDE

Updated: Aug 2014

Supersedes Waiver Guide of Jun 2010

By: Lt Col David Andrus (RAM XV) and Dr. Dan Van Syoc

Reviewed by Lt Col Thomas Stamp, AF/SG consultant for General Surgery and Lt Col Roger Wood,

AF/SG consultant for Hematology/Oncology

### **CONDITION:**

Splenectomy (Aug 2014)

### I. Waiver Consideration.

A history of splenectomy for any cause is disqualifying for FC I/II/III and ATC/GBO/SWA, and requires a waiver. Issuance of a waiver requiring renewal insures that aviators are properly educated, vaccinated and receive prophylactic antibiotics for OPSS throughout their lifetime. Flight surgeons must routinely and emphatically educate their asplenic flyers about OPSS. Creating a waiver in AIMWTS serves as a means to track these patients. This practice assists in preventing severe complications, as studies have shown that registries for splenectomy patients are effective in the prevention of OPSS.<sup>30</sup>

Table 1: Waiver potential for flyers status post splenectomy

| Flying Class (FC)     | Condition*                | Waiver Potential <sup>#</sup> Waiver Authority |
|-----------------------|---------------------------|--|
| I/IA                  | Splenectomy for any cause | Yes<br>AETC                                    |
| II/III<br>ATC/GBO/SWA | Splenectomy for any cause | Yes<br>MAJCOM                                  |

<sup>\*</sup>If the medical condition is also disqualifying, refer to the applicable AFI or waiver guide for guidance. # No indefinite waivers.

AIMWTS review in Aug 2014 revealed 21 waivers submitted for total splenectomy. There were 2 FC I/IA cases, 11 FC II cases, 7 FC III cases, and 1 ATC/GBC cases. The causes for splenectomy were rupture due to mononucleosis, trauma, ITP, splenomegaly, spherocytosis, MEN type 1, Hodgkin lymphoma, and splenic artery torsion. A patient with non-Hodgkin lymphoma (FCII) and a patient with malignant melanoma with splenic metastases to the spleen (FC III) were disqualified; and one member was disqualified for anthropometric reasons.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for splenectomy should include the following:

- A. A complete history describing the cause of splenectomy, the age at splenectomy and response to splenectomy. The history also needs discussion of the postoperative course and must include any reports of DVT, mesenteric venous thrombosis (MVT) or proximal venous thrombosis (PVT).
- B. Documentation of vaccination for pneumococcus, meningococcus, *H. influenza* and viral influenza, prescription of prophylactic antibiotics, type and dose for use in the case of fever and education about the risks of OPSS must be included.
- C. Labs: CBC and lipid panel.
- D. Copies of all operative reports and a statement from treating physician.

# The AMS for <u>waiver renewal</u> for splenectomy should include the following:

- A. Interval history specifically noting any changes in disease course and treatments since the last waiver submission. Included should be a complete review of systems, and specifically include any signs or symptoms of VTE or pulmonary hypertension
- B. Documentation of vaccination status and booster vaccinations given, renewal prescriptions for prophylactic antibiotics and refresher education on the risks of OPSS must be included. Physical examination for VTE and pulmonary hypertension should be done.
- C. Labs: CBC and lipid panel.
- D. Statement of patient condition from treating physician.

### III. Overview.

# **Splenic Function**

The spleen is the body's largest lymphoid organ and processes six percent of the cardiac output. The macrophage-lined sinuses of the red pulp function as filters for senescent and abnormal red blood cells and the repair or polishing of normal red blood cells. The filtering function prevents intravascular hemolysis and release of hemoglobin into the plasma. Circulating hemoglobin due to intravascular hemolysis is also filtered by splenic macrophages. Splenic macrophages process hemoglobin and iron and serve as a store for iron. The white pulp of the spleen consists of germinal centers similar to lymph nodes, but the macrophages are uniquely designed to recognize, trap and process carbohydrate antigens found on blood-borne pathogens without surface opsonins. In addition, the spleen is the major producer of antigen-specific IgM antibody which is important in the early response to infection. The spleen also serves as a large reservoir for platelets, containing up to 30% of the platelet volume. Absence of these important blood and immune monitoring functions places asplenic individuals at risk for life-long infectious and thrombotic complications. <sup>2</sup>

## **Indications for Splenectomy**

Approximately 22,000 total splenectomies are performed annually in the U.S.<sup>3</sup> Common reasons for splenectomy include trauma, hematologic disorders and malignancy. Appreciation for the immunologic and blood monitoring functions of the spleen has resulted in a trend toward splenic preservation in both trauma and hematologic disorders.<sup>4</sup> Up to 70-90% of children and 40-50% of adults with splenic injury are successfully managed non-operatively.<sup>5</sup> Less common conditions requiring splenectomy include splenic cysts due to parasites (hydatid disease) and splenic abscess.

## Hematologic disorders

The following hematologic conditions have commonly led to splenomegaly and/or hypersplenism and a potential splenectomy: idiopathic thrombocytopenic purpura (ITP), thrombotic

thrombocytopenic purpura (TTP), idiopathic autoimmune hemolytic anemia (AIHA), hereditary spherocytosis, hemoglobinopathies such as sickle cell disease and thalassemia, myelofibrosis and myeloid metaplasia, and myeloproliferative disorders such as polycythemia vera and essential thrombocythemia. The last category of patients is considered high risk for thrombotic complications (see Vascular Complications below). <sup>5, 6</sup>

## Malignancy

The malignancies which commonly lead to splenectomy include Hodgkin's disease, non-Hodgkin's lymphoma, chronic myelogenous leukemia, chronic lymphocytic leukemia and pancreatic cancer. The latter is the most common malignancy resulting in splenectomy.<sup>5</sup> There are also epidemiologic studies which show an association between splenectomy and an increased risk of developing cancer.<sup>3</sup>

# Complications of Splenectomy

Acute complications occur in the initial postoperative period and include hemorrhage, subphrenic abscess, pancreatic injury or fistula, and portal or mesenteric vein thrombosis. Late complications include overwhelming postsplenectomy sepsis (OPSS) and thrombosis. Other alterations in blood content and viscosity can also occur and include leukocytosis, thrombocytosis, increased lipid levels, intravascular hemolysis and endothelial dysfunction. The full effect these vascular changes on late vascular complications has not been completely studied or measured.

### Overwhelming Post Splenectomy Sepsis (OPSS)

The absence of the specialized phagocytic immune functions of the spleen places asplenic patients at risk for infection and overwhelming sepsis. The most serious and most common pathogen is *S. pneumonia* which accounts for over half all infections and deaths. Other bacterial pathogens include *H. influenza*, *N. meningitides*, along with the less common bacteria *Capnocytophagia canimorsus* (dog and cat saliva) and *Bordetella homesii*. Severe forms of parasitic infections with malaria and babesiosis, ehrlichiosis and cytomegalovirus have also been documented. OPSS presents with fever and a short prodrome that rapidly progresses to septic shock and diffuse intravascular coagulation. Mortality can be as high as 50-80% and occur within 48 hours of hospital admission.<sup>7,8</sup>

The risk for OPSS applies to all asplenic patients and extends through their lifetime. The risk is higher in children because they lack pre-existing immunity and is estimated at one per 175 patient-years. The risk for adults is highest in the first two years following splenectomy and is estimated at one per 400-500 patient-years. Risk for OPSS also varies by underlying disorder and the reason for splenectomy. Cumulative risk for OPSS after traumatic splenectomy is the lowest at 1.5%; hematologic disorders are next at 3.4% and sickle cell disease and thalassemia are the highest at 15% and 25%, respectively. I

The risk for OPSS can be decreased by a three tiered approach of vaccination, prophylactic antibiotics and education.<sup>8,9</sup> Vaccinations should be given for pneumococcus, *H. influenza* type b, meningococcus, and annual viral influenza. Booster is recommended for pneumococcal vaccine after five years. Meningococcal booster with the conjugate vaccine is recommended if the polysaccharide vaccine was received 3-5 years in the past. Vaccinations should be given at least fourteen days before surgery or fourteen days after surgery when not elective.<sup>10</sup>

Prophylactic antibiotics are given in a daily regimen or empirically for fever. A daily regimen of oral penicillin VK or amoxicillin is recommended for children until age 5 or at least one year following splenectomy. Daily regimens are not recommended in adults except for those who have experienced OPSS as the risk for recurrence is increased six-fold as well as highly immunocompromised adults. Empiric antibiotic therapy for fever is recommended for all asplenic patients. Adult patients should have at least one dose of an anti-pneumococcal antibiotic immediately available if fever and rigors develop and proceed for emergency care without delay. Antibiotic recommendations include amoxicillin-clavulanate (875 mg BID), cefuroxime axetil (500 mg BID), levofloxacin (750 mg QD), moxifloxicin (400 mg) or gemifloxicin (320 mg QD). Prophylactic antibiotics have been shown to decrease the incidence of infection by 47% and the mortality by 88%. 7, 10

Education is the third arm of OPSS prevention. Studies have shown an alarming lack of unawareness among asplenic patients marked by failure to comply with vaccine and antibiotic recommendations. Patients should be counseled before and after splenectomy and be encouraged to wear a medical alert bracelet. Registries for asplenic patients may increase compliance and improve outcomes.<sup>8, 9</sup>

## Vascular Complications

Over the past 30 years, the medical literature has steadily accumulated evidence of a life-long increased risk of vascular complications after splenectomy. Vascular complications include thrombosis, thromboembolism, vascular smooth muscle remodeling, vasospasm or atherosclerosis and occur on the arterial and venous sides of the circulation. The risk appears to vary by cause for splenectomy and underlying disease states, but none are without increased risk. The highest risk is in those with underlying myeloproliferative disorders or in hematologic disorders with on-going intravascular hemolysis. Venous thromboembolism appears to be more common than arterial. Currently, there are no clear guidelines for prophylactic anti-platelet or anticoagulation medications in splenectomized patients.<sup>3</sup>

The pathophysiologic mechanisms for vascular complications are multifactorial and include hypercoagulability, platelet activation, endothelial activation, vascular remodeling, and increased lipid levels.<sup>3</sup> Reactive thrombocytosis may occur in up to 75% of splenectomized patients but is not consistently associated with thrombosis.<sup>11-13</sup> Chronic platelet activation is more likely and has been shown to be increased in splenectomized patients with pulmonary hypertension.<sup>14</sup> Hypercoagulability may also be related to increased cellular microparticles and damaged red blood cells that activate the vascular endothelium.<sup>3, 15</sup> In addition, plasma levels of hemoglobin may be increased due to intravascular hemolysis and loss of splenic hemoglobin uptake. Increased free hemoglobin has direct inflammatory and cytotoxic effects on endothelium and scavenges nitric oxide needed for vascular smooth muscle relaxation.<sup>4, 16</sup> Finally, splenectomy may increase lipid levels as evidenced by animal studies.<sup>17</sup>

## Venous thromboembolism (VTE)

Portal and mesenteric vein thrombosis most commonly occurs within the first few weeks after splenectomy. The incidence may be as high as 50%, but symptomatic thrombosis occurs in approximately 5-10% of cases. <sup>12, 18</sup> Predisposing factors include thrombocytosis (platelet count >  $650 \times 10^3/\mu l$ ), greater spleen weight, myeloproliferative disease and possibly laparoscopic technique. <sup>10, 18</sup> Most patients respond to systemic anticoagulation with recannulation in 90% (18),

but death can occur in 5% of cases. 11 Survivors are at risk for portal hypertension. 12 Prophylactic postoperative anticoagulation should be considered in patients with hematologic disorders, but intensity and duration has not been determined. 19

Late venous thromboembolic events include deep venous thrombosis and pulmonary embolus. In two mortality studies, splenectomized patients for all reasons had increased mortality due to venous thromboembolic events (VTE). In 1996 Linet et al reported a rate of 0.31% (4/1297) and Standardized Mortality Ratios of 4.8 (1.3-12.3) in trauma patients who died more than one year after the splenectomy. In 1989 Pimpl et al reported an increased mortality related to pulmonary embolus in 35.6% of splenectomized patients compared to 9.7% of controls (p<0.001). In 2008 Schilling et al demonstrated an increased lifetime risk of venous thromboembolic events (VTE) in splenectomized HS patients as compared to unaffected controls and spleen-in HS patients (see Table 1). The incidence did not increase above controls until after 30 years of age, then increased incrementally: 3-6% at age 30, 5-7% at age 40, 10-13% at age 50 and 19-20% at age 70. Lastly, in 2005 Jaïs et al reported that 54% of splenectomized patients with pulmonary hypertension had a history of VTE at least one year after splenectomy.

### Arteriothrombosis

The first suggestion of increased arterial thrombotic complications was reported by Robinette and Fraumeni in 1977 who evaluated the causes of mortality in WWII veterans following traumatic splenectomy.<sup>23</sup> They reported an excess mortality due to ischemic heart disease compared to controls (RR 1.857, p<0.05). Schilling confirmed this increased risk in splenectomized HS patients in 1997 and 2008.<sup>24</sup> By age 70, the cumulative incidence of first arterial events (MI, stroke, coronary artery surgery, carotid artery surgery) was 32% in males and 22% in females with a hazard ratio of 7.15 (2.81-17.2, p<0.0001). The incidence rate did not increase above controls until after 50 years of age. Other reported arterial events in this population included acute ischemic optic neuropathy and pulmonary hypertension.<sup>22</sup> Linet also showed an association of older age with increased cerebrovascular events (3.7%, SMR 1.7).<sup>20</sup> ITP patients treated with splenectomy were found to have increased platelet activation associated with accelerated small vessel cerebrovascular disease and vascular dementia.<sup>25</sup>

## Pulmonary hypertension

The most compelling evidence for thrombotic complications after splenectomy is the association of splenectomy with pulmonary hypertension. Splenectomy is now considered an independent risk factor for the development of chronic thromboembolic pulmonary hypertension (CTEPH).<sup>24</sup> Although splenectomy has been associated with CTEPH, the incidence of CTEPH after splenectomy for all causes has not been determined by prospective studies. A case-control study by Jaïs showed that CTEPH developed in a mean of 16 years after splenectomy (range 3-35 years) and another study by Hoeper showed a range of 4 to 34 years after splenectomy. CTEPH developed in patients for all causes of splenectomy. The series by Jaïs included a majority of trauma splenectomies (12/22) with a mean age of 34 years at the time of surgery. Other causes of splenectomy included ITP and HS. Selective series in thalassemia and Gaucher's disease have also showed an association of splenectomy with pulmonary hypertension. Lastly, splenectomized patients who develop CTEPH have higher surgical mortality, persistent pulmonary hypertension, and show recurrent disease after transplantation. <sup>13, 26, 27</sup>

### IV. Aeromedical Concerns.

Aeromedical concerns stem from the underlying condition for which the splenectomy was performed and the lifelong risk of overwhelming sepsis and vascular complications. Aeromedical concerns of the underlying medical conditions are discussed in the appropriate waiver guide for that particular condition. The lifelong risk of overwhelming sepsis and vascular complications apply to all splenectomized patients regardless of cause.

OPSS can present acutely and progress rapidly even within a few hours of onset which may result in incapacitation or the need to divert the flight. The splenectomized aviator should not delay treatment with antibiotics and care in an appropriate medical facility. Aviators should carry at least one dose of prophylactic antibiotics to take if symptoms occur while in flight. The incidence of OPSS ranges from 1.5% for trauma splenectomies to 25% in hematologic disorders and is highest in the first three years after splenectomy. Vaccination, antibiotics and education is imperative to reduce the risk of OPSS in aviators to acceptably low levels.

The aeromedical impact of the lifelong risk of vascular complications is more difficult to determine not only because the risk has not been well-defined but also because there are no clear recommendations for anti-platelet or anticoagulation prophylaxis. Any venous or arterial thromboembolic event could result in sudden incapacitation such as deep venous thrombosis and pulmonary embolus (DVT/PE). Restricted movement in the cockpit on long flights could increase the risk of developing DVT/PE. The incidence of venous thromboembolic events is greatest in the early postoperative period and remains below 10% for several years but appears to increase as the patient gets older. The incidence of arterial events appears to increase after 50 years of age. 22

Splenectomy has been strongly associated with pulmonary hypertension. Unfortunately, the overall incidence of pulmonary hypertension in splenectomized patients has not been reported, but is likely very low. It can develop as early as two years or as late as 34 years after splenectomy and may be more frequent in those patients with a history of VTE. By the time of presentation, damage to the pulmonary vasculature is already extensive. Common symptoms include exertional dyspnea, fatigue, weakness, anginal chest pain and syncope. These symptoms are due to impaired oxygen transport and reduced cardiac output which is not compatible with aviation duties. In addition, hypoxia as may be present in the aviation environment is a potent stimulant of pulmonary vasoconstriction and may worsen the development of disease. Pulmonary artery endarterectomy may be curative, but splenectomy patients tend to have distal disease not amenable to surgery. Aviators with splenectomy should be evaluated regularly for any signs or symptoms of pulmonary hypertension and have further testing if pulmonary hypertension is suspected.

| ICD-9 codes for splenectomy |  |
|-----------------------------|--|
| 41.5                        | Operations on bone marrow and spleen; total splenectomy                    |
| 41.43                       | Operations on bone marrow and spleen; excision or destruction of lesion or |
|                             | tissue of spleen; partial splenectomy                                      |

| ICD-10 codes for splenectomy |   |  |
|------------------------------|---|--|
| 07TP0ZZ                      | Resection of spleen, open approach                    |  |
| 07TP4ZZ                      | Resection of spleen, percutaneous endoscopic approach |  |
| 07BP0ZZ                      | Excision of spleen, open approach                     |  |
| 07BP0ZZ                      | Excision of spleen, percutaneous approach             |  |
| 07BP0ZZ                      | Excision of spleen, percutaneous endoscopic approach  |  |

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## Spondylolysis and Spondylolisthesis (Feb 2019)

Reviewed: Lt Col Ross Semeniuk (RAM 2020) Dr. Dan Van Syoc (ACS waiver guider coordinator), Col Brandon Horne (AF/SG consultant for orthopedic surgery), and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

# **Significant Changes:**

Table change

### I. Waiver Consideration

Spondylolysis is a defect involving the pars interarticularis of the vertebrae. Spondylolisthesis is a condition in which there is anterior slipping of a vertebrae. The most common location for these conditions occurs at the lower lumbar vertebrae.

Symptomatic spondylolysis or spondylolisthesis that requires repeated hospitalizations, duty restrictions, or frequent absences from duty is disqualifying for all flying classes, ATC, GBO and SWA duties, as well as for retention. Spondylolysis and spondylolisthesis are often associated with other spinal pathologies (e.g. spina bifida, disc protrusion, spinal stenosis, disc disease) that are also disqualifying.

If spondylolysis or spondylolisthesis is treated with surgery, refer to the waiver guide on herniated nucleus pulposus (HNP) and spinal fusion for additional waiver considerations.

Table 1: Waiver potential for Spondylolysis and/or Spondylolisthesis

| Flying Class               | Condition  | Waiver Potential                                | ACS               |
|----------------------------|--|---|-------------------|
| (FC)                       |  | Waiver Authority                                | Review/Evaluation |
| I/IA                       | Symptomatic spondylolysis<br>and/or Symptomatic grade I/II<br>spondylolisthesis  | Yes<br>AETC                                     | No                |
|                            | Symptomatic spondylolysis<br>and/or symptomatic<br>spondylolisthesis, or<br>asymptomatic spondylolisthesis<br>grade III or higher (treated or not)                                       | No<br>AETC                                      | No                |
| II/III<br>ATC, GBO,<br>SWA | Symptomatic spondylolysis and/or symptomatic spondylolisthesis controlled only with exercise or NSAIDs   | Yes <sup>1, 2,3</sup><br>MAJCOM                 | No                |
|                            | Spondylolysis and/or spondylolisthesis treated with surgery  | Maybe <sup>2</sup><br>AFMRA/MAJCOM <sup>4</sup> | No                |
|                            | Spondylolysis or<br>spondylolisthesis, when<br>symptoms and associated<br>objective findings require<br>repeated hospitalization, duty<br>restrictions or frequent absences<br>from duty | Maybe<br>AFMRA                                  | No                |

- 1. If spondylolisthesis is grade III or greater waiver unlikely for untrained FC II and FC III individuals.
- 2. Waiver unlikely for untrained FC II and FC III personnel.
- 3. Not disqualifying for ATC and GBO personnel.
- 4. See HNP and spinal fusion waiver guide.

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. History Presentation, course, and a thorough back history including:
  - a. any adolescent sports injuries; and
  - b. vehicular accidents.

If aviator had past or present symptoms, document nature of pain and treatment received.

- 2. Orthopedic spine or neurosurgical consultation report.
- 3. Diagnostic imagining –X-ray (AP, LAT, obliques), and CT/MRI results.

- 4. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 5. Current physical examination spine (range of motion), extremities (range of motion, strength, sensation, and reflexes).
- 6. Any other pertinent information. MEB result, if required.
- 7. If the above items are not available, it is necessary to explaining reasoning to the waiver authority.

## B. Renewal Waiver Request:

- 1 Interval history Describe circumstances of any back pain, severity, limitations, treatment, duration of symptoms, and DNIF period; current activity level.
- 2 Current physical examination spine (range of motion), extremities (range of motion, strength, sensation, and reflexes).
- 3 Diagnostic imagining –X-ray (AP, LAT, obliques) if recurrent symptoms.
- 4 Orthopedic spine or neurosurgical consultation report.
- 5 MEB updates, if applicable.
- 6 If the above items are not available, it is necessary to explaining reasoning to the waiver authority.

### **III. Aeromedical Concerns**

Spondylolisthesis and spondylolysis represent structural abnormalities of the lumbar spine and may be manifested by low back pain. Such pain is unlikely to cause sudden incapacitation but can cause distraction during flight operations.

Spondylolysis may be caused by a stress fracture and lead to occasional or chronic low back pain. Additionally, the affected portion of the spine may be particularly vulnerable to accelerative stress.

Spondylolisthesis can be secondarily caused by degenerative disc disease or spondylolysis. It may also cause low back pain as well as sciatica. The aviator's response to continued exposure to vibration and accelerative forces should be considered. However, an AF Aerospace Medical Research Laboratory report on spinal column considerations for flight physical standards noted that there were no proven demonstrations in which the aggravation of spondylolisthesis was shown in the course of time.

A Feb 2019 review of AIMWTS revealed 193 members with a waiver disposition for spondylolysis or spondylolisthesis. Of this total, 31 were disqualified. Breakdown of the cases revealed: 8 FC I/IA cases (2 disqualified), 93 FC II cases (8 disqualified, of which 5 had a previous waiver), 2 RPA pilot cases, 80 FC III cases (18 disqualified, of which 7 had a previous waiver), 7 ATC/GBC cases (3 disqualified), and 3 MOD cases. The majority of the disqualified cases were due to vertebral concerns.

| ICD-9 Codes for Spondylolysis and Spondylolisthesis |  |
|---|--|
| 738.4   | Acquired spondylolisthesis/spondylolysis |
| 756.11  | Spondylolysis (congenital)               |
| 756.12  | Spondylolisthesis (congenital)           |

| ICD-10 Codes for Spondylolysis and Spondylolisthesis |                                    |
|--|------------------------------------|
| M43.10   | Spondylolisthesis site unspecified |
| M43.00   | Spondylolysis, site unspecified    |
| Q76.2  | Congenital spondylolisthesis       |

## **IV. Suggested Readings**

- 1. North American Spine Society. *Diagnosis and treatment of degenerative spondylolisthesis*. 2<sup>nd</sup> edition. 2014. Retrieved from:
- https://www.spine.org/Portals/0/Documents/ResearchClinicalCare/Guidelines/Spondylolisthesis.pdf ?ver=2016-04-12-134623-410
- 2. Evans N and McCarthy M. Management of symptomatic degenerative low-grade lumbar spondylolisthesis. EFORT Open Rev, 2018 Dec 19; 3(12): 620-31.
- 3. Syrmou E, Tsitsopoulos PP, Marinopoulos D, et al. Spondylolysis: a review and reappraisal. Hippokratia, 2010; Jan; 14(1): 17-21.
- 4. Kazarian LE and Belk WF. (1979). Flight physical standards of the 1980's: spinal column considerations. Aerospace Medical Research Laboratory (AMRL) Technical Report (TR)-79-74; October 1974.

## **Substandard Stereopsis (Formerly Defective Depth Perception) (Mar 2020)**

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

New Ground Based Operator (GBO) Standards. MSD C81

#### I. Waiver Consideration

All FC I/IA with VTA-DP or OVT-DP failure (unable to accurately read line B) who are otherwise qualified are required to either have an evaluation or have the case reviewed by the Aeromedical Consultation Service (ACS). The new passing standard for stereopsis is 40 arc sec (OVT-DP line "B").<sup>1</sup>

All FC II and FC III aircrew positions that require depth perception to safely clear their aircraft or self (e.g. free fall) from objects or other aircraft in the air or on the ground within 200 meters (scanner duties), e.g. boom operators, flight engineers, loadmasters, who newly fail the annual required depth perception testing (VTA or OVT), or who have failed in the past (using the 40 arc sec standard) and never been evaluated at the ACS for defective stereopsis are required to have an ACS review and possible evaluation before granting of waiver. Monofixation/Microtropia management and the Prospective Defective Stereopsis management groups have been closed as the requisite data has been collected and interpreted.

At the annual Flight Qualification exam (PHA); if the trained aviator has previously failed the VTA or OVT, has undergone a prior ACS review or evaluation with existing **indefinite** waiver, and can currently either pass the VTA or OVT, achieve a passing score 4/4 (60 arc sec) on the AO Vectograph distance stereopsis test, or achieve a previously waivered baseline score on the AO Vectograph (as determined by the ACS); no further workup is needed until next Flight Qualification exam (PHA). If depth perception capability has declined from the previously waivered level or if binocular fusional control has diminished (i.e., onset of diplopia), previous waiver is nullified and full workup should be accomplished as outlined below in the Information Required for Waiver Submission section.

Defective depth perception requirement is outlined in the AFECD/AFOCD and generally is not waiverable for initial FC III applicants for the following career fields: 1A0 (Boom Operators), 1A1 (Flight Engineers), 1A2 (Loadmasters), 1A3 (Airborne Mission System Operators), and 1A7.

There is no depth perception standard for ATC, GBO, or SWA personnel. Initial RPA Pilot applicants will meet FAA Third Class Medical Certificate standards for URT if they do not have a history of strabismus or diplopia. While not disqualifying for SWA personnel, Tactical Air Control Party (TACP) (1C4X1) and Air Liaison Officers (13LX) are required to meet depth perception standards for training with sister services.

Depth perception (40 arc sec) is the standard for FCI/IA, FCII, and FCIII. If the depth perception standard is not met, a waiver will be required. More extensive work up for waiver submission will only be required for FC III and GBO career fields that carry a depth perception requirement outlined in the AFECD/AFOCD as listed above as well as FC I/IA and FC II.

**Table 1: Waiver potential for Defective Depth Perception** 

| Flying Class (FC)   | Waiver Potential | Required ACS      |
|---------------------|------------------|-------------------|
|                     | Waiver Authority | Review/Evaluation |
| FC I/IA             | Yes <sup>2</sup> | Yes               |
|                     | AETC             |                   |
| FC II               | Yes <sup>2</sup> | Yes               |
| FC III <sup>1</sup> | MAJCOM           |                   |
| SWA <sup>3</sup>    | Yes <sup>2</sup> | No                |
|                     | MAJCOM           |                   |
| ATC/GBO/OSF         | N/A              | N/A               |

<sup>1.</sup> Aircrew positions that require depth perception (scanner duties), e.g. boom operators, flight engineers, loadmasters, etc. will require work up for waiver submission.

Previous retrospective study conducted by the Ophthalmology Branch of the ACS found 524 aviators were evaluated for defective stereopsis/depth perception. The final ACS diagnosis in this group ranged from a vergence or phoria in 31%, microesotropia in 29%, monofixation in 24%, microexotropia in 10% and vertical microtropia in 1%.<sup>2</sup>

A 2017 review of the ACS Defective Stereopsis (Prospective) Study Group from 1997 until the present, found 753 subjects evaluated. Of those, 540 were analyzed with 213 excluded from analysis for not having follow-up exams (178), not meeting study criteria (32), or uninterpretable findings (3). Of the 540 analyzed, 536 documented stability over an average period of 7.7 years (0.7-18.8). There were 4 subjects who decompensated over average period of 6.6 years (0.9-10.9). Therefore, 4 of 540 (0.7%) decompensated over 7.7 years for an annual rate of <0.1%.

## II. Information Required for Waiver Submittal

The most common cause of an acquired depth perception defect is uncorrected refractive error. Depth perception testing should not be attempted until optimal correction has been achieved. Failure of depth perception with best corrected visual acuity is disqualifying, but may be considered for waiver.

After initial ACS Evaluation or Review for stereopsis failure, an indefinite waiver may be recommended. Annual routine PHA demonstrating a change in stereopsis status will nullify existing waiver, and require ACS review or evaluation.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using the best current clinical guidelines/recommendations. Underlying conditions such as microtropia, monofixation syndrome,

<sup>2.</sup> If spectacles were needed to pass depth perception testing, regardless of unaided visual acuity (e.g. 20/20) then spectacles are required for aviation duties, to meet depth perception standards.

<sup>3.</sup> Further workup only required for following career fields: 1C4X1 and 13LX.

and anisometropia that are identified during evaluation by the local optometrist or ophthalmologist should be listed as a separate disqualifying condition along with a diagnosis of defective stereopsis. It should be noted that if after a thorough examination no underlying diagnosis is found, a disqualifying diagnosis of defective stereopsis is sufficient for AMS submission.

A complete AMS with a local ophthalmologist/optometrist work-up to include all of the following is required for **indefinite waiver** consideration.

- 1. Complete ocular history noting particularly any history of eye patching, spectacle wear at an early age, strabismus, eye surgery and previous depth perception testing performance.
- 2. Ductions, versions, cover test and alternate cover test in primary and six cardinal positions of gaze.
- 3. Optimal refraction with further testing, including repeat VTA-DP or OVT-DP, to be accomplished with best optical correction of any refractive errors, regardless of unaided visual acuity.
- 4. AO Vectograph stereopsis test at 6 meters (4 line version) (distant stereopsis)\*
- 5. AO suppression test at 6 meters.
- 6. Randot or Titmus stereopsis test (near stereopsis tests).
- 7. Red lens test.
- 8. Four-diopter base-out prism test at 6 meters.
- 9. Direct/indirect macula and optic nerve exam.
- 10. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

\*Note: Use only the American Optical (AO) version of the vectograph projection slide graded in 60 arc sec increments (60, 120, 180, 240 arc sec).

#### **III. Aeromedical Concerns**

Stereopsis is generally not considered to be a factor in the perception of depth beyond 200 m, as monocular cues tend to prevail at these distances. In aviation, accurate perception of spacing or depth within 200 m is critical in a number of situations, such as aerial refueling, formation flying, holding hover rescue type operations, taxiing, and parking. Stereopsis also facilitates closure maneuvers and rejoins. Microtropia and monofixation syndrome may be intermittent in nature and susceptible to decompensation in the aerospace environment due to such exposure as relative hypoxia and fatigue over time.

Following members from 1997 to present in the Defective Stereopsis (Prospective) Study Group, there was an annual risk of decompensation of <0.1% per year. While there is a chance of decompensation, it is well below the acceptable aeromedical risk of 1%. Members will continue to have their depth perception monitored with the annual PHA.

Fourth cranial nerve (superior oblique) palsy, as with other forms of vertical phorias and tropias, has been shown by ACS experience to more likely decompensate over time in aircrew with resultant diplopia than the horizontal microtropias. Therefore a waiver for this diagnosis will generally NOT be recommended.

A review of AIMWTS through Jun 2018 showed 5438 aeromedical summaries containing a diagnosis of substandard stereopsis. There were a total of 904 cases disqualified, the majority which were either for another unrelated diagnosis or for untrained assets. There were 888 FC I/IA cases, 1442 FC II cases, 163 RPA pilot cases, 2713 FC III cases, 213 ATC/GBC cases, and 19 MOD cases.

| ICD-9 Code for Defective Stereopsis (Depth Perception) |                                     |
|--|-------------------------------------|
| 368.3  | Other disorders of binocular vision |

| ICD-10 Codes for Defective Stereopsis (Depth Perception) |  |
|--|--|
| H53.30   | Unspecified disorder of binocular vision |
| H53.34   | Suppression of binocular vision          |

## **IV. Suggested Readings**

- 1. Steinman SB, Steinman BA, Garzia RP. (2000) Foundations of Binocular Vision: A Clinical perspective. McGraw-Hill Medical.
- 2. Parsons, M, Wright S, Ellis, J. Stereopsis testing in the US Air Force: Where we have been and where we are going. Ramstein Aerospace Medicine Summit NATO STO Technical Course, 2018, poster session.
- 3. Hunt MG, Keech RV. Characteristics and course of patients with deteriorated monofixation syndrome. J AAPOS, 2005; 9: 533-6.

## Suicide, Attempted or Suicidal Behavior (Feb 2019)

Reviewed: Lt Col Kevin F. Heacock (Chief, ACS Neuropsychiatry Branch), Dr. Dan Van Syoc (Deputy Chief, ACS), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Restructured Waiver Guide, Defined Clinical Stability, Updated Table 1 and References

#### I. Waiver Consideration

For aviators, a history of Attempted Suicide or Suicidal Behavior is disqualifying for all classes of flyers, to include ATC/GBO and SWA personnel (MSD Q36). To be eligible for waiver, it is recommended the member display a period of **Clinical Stability for 6 months** after reaching "Best Baseline" functioning. "Best Baseline" is reached when the aviator's Mental Health Provider (MHP) determines the symptoms of the diagnosis are no longer causing clinically significant distress or impairment and the aviator demonstrates adequate function in social, occupational, and other important areas for functioning. Once "Best Baseline" is reached treatment adjustments can still be made, including medication changes, without restarting the period of clinical stability as long as the aviator's levels of distress, impairment, or functioning have not deteriorated to a point which the MHP determines is clinically significant.

Table 1: Waiver potential for aviators with history of Attempted Suicide or Suicidal Behavior

| Flying Class (FC) | Waiver Potential      | Waiver Authority | ACS Review or Evaluation |
|-------------------|-----------------------|------------------|--------------------------|
| FC I/IA           | Maybe <sup>1, 3</sup> | AETC             | Yes <sup>2</sup>         |
| FC II/III         | Maybe <sup>1, 3</sup> | MAJCOM           | Yes <sup>2</sup>         |
| ATC/GBO/SWA       | Maybe <sup>1, 3</sup> | MAJCOM           | Yes <sup>2</sup>         |

<sup>1.</sup> Underlying conditions that exacerbated suicidal behavior must be treated successfully and the aviator or aviator candidate must not have a higher risk of suicidal behavior than does the general military population.

### II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

## A. Initial Waiver Request:

- 1 See Mental Health Waiver Guide Checklist
- 2 If the local base is unable to provide all required items, they should explain why, explaining reason to waiver authority.

<sup>2.</sup> ACS review/evaluation if requested by Waiver Authority for initial FC I/IA, FC II, FC III, ATC, GBO, and SWA applicants.

<sup>3.</sup> No indefinite waivers.

## B. Renewal Waiver Request:

- 1. See Mental Health Waiver Guide Checklist
- 2. If the local base is unable to provide all required items, they should explain why, explaining reason to waiver authority.

#### **III. Aeromedical Concerns**

Suicidal behavior must always be taken seriously in any Airman, especially those who are required to meet enhanced medical standards. Not only is the individual aviator at risk, but the safety of others in the air and on the ground must be considered, as well as the conservation of valuable national assets, and the implications of access to nuclear and other weapons.

Especially concerning is the performance requirements of military aviators for readiness and mission completion. While suicide behavior may be a single act, it often represents a distinct, overt pattern of behavior in a long, debilitating process. By and large, aviators are known to demonstrate emotional composure and may deny, suppress and/or otherwise defend against emotional turmoil. Because of this, the need for peers and flight surgeons to carefully monitor aircrew for early signs of emotional conflict, despair, and intimate relationship deterioration is essential.

A history of attempted suicide or suicidal behavior is disqualifying (referred to generally as suicidal behavior in the waiver guide). All suicidal ideation, self-destructive actions or overt suicidal attempts by aviators require immediate DNIF action and mental health evaluation, including voluntary or involuntary hospitalization if psychiatrically indicated. Such decisions are based on many factors besides the specific diagnosis, including the patient's intent to die, the lethality of the method chosen, availability of means, the energy put into the attempt, the role of possible substances, the circumstances of the rescue (i.e., found by accident vs. found after hints, phone call, presentation to ER, etc.), and the emotional support systems available to the aviator. Of great concern in aviators with suicidal ideation is the possibility of suicide by aircraft, which is rare, but has occurred in civilian and military settings. Appropriate action should be taken in regard to the Personnel Reliability Program, if applicable. If the precipitating event involved acute or chronic alcohol misuse, an additional waiver will be managed IAW AFI 48-123 and AFI 44-121, *Alcohol and Drug Abuse Prevention and Treatment (ADAPT) Program*.

Suicide is defined as "the act of ending one's own life." Suicide often results from extreme emotional pain coupled with the belief that cessation of the mental suffering will only be achieved by no longer living. Suicidal ideation refers to ruminative thoughts of ending one's life; suicide plan refers to the identified method and preparation of ending one's life; and suicide attempt refers to self-injurious behavior with an intent to die. Another closely related behavior is non-suicidal self-injury which involves cutting, burning, severe scratching, and hitting. Severe cases of non-suicidal self-injury may involve bone breaking and ocular enucleation. The National Institute of Mental Health (NIMH) states that most suicide attempts are expressions of extreme distress, not attempts to garner attention. The NIMH emphasizes that a person who appears suicidal should not be left alone and requires immediate mental-health treatment.

The overall rate for suicide within the general U.S. population is 13.4 per 100,000 people and is the tenth leading cause for death. Those attempting suicide most often engage in medication overdose,

while suicide completers most often die from self-inflicted gunshot wounds or strangulation. Demographic analyses of non-military populations indicate that women are three times more likely to attempt suicide than men, but men are three times more likely to successfully complete suicide (largely associated with the method of suicide employed).

Suicides committed by members of the military has raised concerns among policymakers, military leaders, and the population at large. The number of suicides among all active duty members was 145 in 2001 and began a steady increase until more than doubling to 321 in 2012, the worst year in recent history for service members killing themselves. The suicide rate for the Army in 2012 was nearly 30 suicides per 100,000 soldiers, well above the national rate. In 2015, there were 266 active duty suicide: 64 in the Air Force (AF), 120 in the Army, 39 in the Marine Corps, and 43 in the Navy.

Suicide remains a major public health problem within the AF and the AF has continually tracked suicides of Airmen since the 1980s. From 1990-1994, rates of AF suicides increased from 10.0 to 16.4 per 100,000, accounting for 23% of all deaths among active duty personnel. In response to this observed rise, a population based program aimed at preventing and reducing stigma was implemented within the AF community; a 33% relative risk reduction was found in those exposed to the program. As part of the AF's 2002 initiative, the Air Force Guide for Managing Suicidal Behavior was established for use in outpatient behavioral healthcare settings. The Guide was most recently updated in 2014. Over the past decade, there have been several spikes in AF suicide rates, with the latest observed in 2010 (15.5 per 100,000). Despite this, the average suicide rate for the AF (10.7 per 100,000) has remained the lowest among all service components from 2001-2009 and has been substantially lower than demographically adjusted civilian rates for the same time period, however, it is still a concern.

Factors contributing to suicidal ideation include distressing life circumstances combined with feelings of hopelessness or helplessness, a recent significant emotional loss, a history of suicide in a family member or close associate, substance abuse, the presence of a psychiatric disorder, and chronic or terminal illness. Risk factors in the US military population have been found to include being on an SSRI, relationship problems, financial challenges, legal problems and substance misuse. In a study comparing suicide non-completers vs suicide completers in the AF, non-completers were likely to be single, never married, and younger (under 24 years old). Completers tended to be older, married and had relationship problems. The overall rate for officers has consistently been lower than that of enlisted members.

From the current known information about aviator suicide, the incidence is small, and probably much less than most other military or civilian occupational groups. Between 2003 and 2012 there were 2,758 fatal aviation accidents. The National Transpiration Safety Board (NTSB) determined that eight were aircraft assisted suicides. All pilots involved were male with a median age of 46 years. Four of the eight pilots were positive for disqualifying substances. Specifically, four pilots tested positive for alcohol, one for benzodiazepines, two positive for unapproved antidepressants, and two were positive for diphenhydramine. Six of the eight had reported thoughts of suicide, attempted suicide before and/or left a note. Additionally, 88% had experienced domestic problems, 13 % had legal issues, and 25% suffered from depression.

AIMWTS review in Feb 2019 revealed 127 cases submitted with a diagnosis of suicide attempt/behavior/ideation. There was a disposition of disqualified in 77 of the cases. Breakdown of the cases revealed: 9 FC I/IA (6 disqualified), 14 FC II (7 disqualified), 2 RPA Pilot (2 disqualified), 68 FC III (38 disqualified), 25 ATC/GBC (17 disqualified), and 9 MOD, (3 disqualified).

| ICD-9 codes for Attempted Suicide or Suicidal Behavior |                               |  |
|--|-------------------------------|--|
| E950   | Suicide attempt               |  |
| 300.9  | Unspecified neurotic disorder |  |

| ICD-10 codes for Attempted Suicide or Suicidal Behavior |   |
|---|---|
| T14.91  | Suicide attempt                           |
| F48.9   | Nonpsychotic mental disorder, unspecified |
| F99   | Mental disorder, not otherwise specified  |

## **IV. Suggested Readings**

- 1. Patterson JC, Jones DR, Marsh RW and Drummond FE. Aeromedical Management of U.S. Air Force Aviators Who Attempt Suicide. Aviat Space Environ Med, 2001; 72(12): 1081-85.
- 2. Wu AC, Donnelly-McLay D, Weisskopf MG, et al. Airplane pilot mental health and suicidal thoughts: a cross-sectional descriptive study via anonymous web-based survey. Environ Health, 2016; 15(1): 121.
- 3. Vuorio A, Laukkala T, Navathe P, et al. Aircraft-Assisted Pilot Suicides: Lessons to be Learned. Aviat Space Environ Med, 2014; 85(8): 841-46.
- 4. Kenedi C, Friedman SH, Watson D, and Preitner C. Suicide and Murder-Suicide Involving Aircraft. Aerosp Med Hum Perform, 2016; 87(4): 388-96.
- 5. Nock MK, Borges G, Bromet EJ, et al. Suicide and Suicidal Behavior. Epidemiol Rev, 2008; 30(1): 133-54.
- 6. Kerr PL, Muehlenkamp JJ, and Turner JM. Nonsuicidal Self-Injury: A Review of Current Research for Family Medicine and Primary Care Physicians. J Am Board Fam Med, 2010; 23(2): 240-59.
- 7. Kochanek KD, Murphy SL, Su J, et al. Deaths: Final Data for 2014. National Vital Statistics Reports, 65(4), June 30, 2016.
- 8. Franklin K. Department of Defense Quarterly Suicide Report: Calendar Year 2016 2nd Quarter.
- 9. Department of the US Air Force. Air Force Guide For Suicide Risk Assessment, Management, and Treatment, June 27, 2014.
- 10. Lollis BD, Marsh RW, Sowin TW, and Thompson WT. Major Depressive Disorder in Military Aviators: A Retrospective Study of Prevalence. Aviat Space Environ Med, 2009; 80(8): 734-37.
- 11. Hyman J, Ireland R, Frost L, and Cottrell L. Suicide Incidence and Risk Factors in an Active Duty US Military Population. Am J Public Health, 2012; 102: S138-46.
- 12. Lewis RE, Forster J, Whinnery JE and Webster N. Aircraft-Assisted Pilot Suicides in the United States, 2003-2012. Civ Aviation Med Institute, 2014.

### WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of Dec 2013

By: Dr. Dan Van Syoc

Reviewed by: Dr. Edwin Palileo and Lt Col Eddie Davenport (Chief Cardiologist ACS), and

AFMSA staff

#### **CONDITION:**

Supraventricular Tachycardia (Jan 2018)

#### I. Waiver Considerations.

Per MSD H9, SVT is disqualifying for all classes of flying duties and for retention in the Air Force (this covers those individuals in the ATC, GBO and OSD programs). An ACS evaluation may be required, depending on the aviation duty, SVT characteristics or specific concerns in an individual case. SVT associated with hemodynamic symptoms will typically not be considered for waiver, unless successful ablation has been performed. Palpitations are not considered to be a hemodynamic symptom. A single episode of asymptomatic nonsustained SVT of 3-10 beats duration will typically be recommended for indefinite waiver for all aviation classes after ACS review. For recurrent episodes of asymptomatic nonsustained SVT or a nonsustained SVT episode longer than 10-beats duration, an ACS evaluation will be required, with expectation of waiver for FC II/III and RPA pilots. Waiver for FC I/IA and untrained FC II/III will be considered on a caseby-case basis depending primarily on characteristics of the nonsustained SVT. A single episode of sustained SVT without hemodynamic symptoms may be considered for FC II, III, or GBO waiver without ablation, on a case-by-case basis. Recurrent sustained SVT is disqualifying without waiver unless successful ablation is performed. SVT treated with antiarrhythmic medication for suppression is disqualifying without waiver. Table 1 is a summary of the clinical manifestations and most common requirements for the separate flying class (FC) duties. Most cases of SVT for ATC, GBO, and SWA personnel will likely be recommended for a waiver unless there is significant hemodynamic compromise. For cases where ablation is part of treatment, please also refer to waiver guide on "Radiofrequency Ablation (RFA) of Tachyarrhythmias".

Table 1. Summary of Supraventricular Tachycardia (SVT) and ACS Requirements.

| SVT (symptoms refers to                                   | Flying Class                      | Waiver     | Required ACS   |
|---|-----------------------------------|------------|----------------|
| hemodynamic symptoms)                                     |                                   | Potential/ | Review and/or  |
|   |                                   | Waiver     | ACS Evaluation |
|   |                                   | Authority  |                |
| Asymptomatic, single episode of                           | FC I/IA/initial FC                | Yes#       | ACS review     |
| 3-10 beats duration                                       | II/GBO/ATC, & ATC                 | AETC       |                |
|   | FC II/III, & ATC                  | Yes#       |                |
|   |                                   | MAJCOM     | ACS review     |
|   | GBO/SWA                           | Yes#       |                |
|   |                                   | AFMSA      | ACS review     |
| Asymptomatic, recurrent                                   | FC I/IA/initial FC II/            | Maybe      | ACS evaluation |
| nonsustained SVT or single episode nonsustained SVT >10   | GBO/ATC                           | AETC       |                |
| beats duration  | FC II/III & ATC/GBO               | Yes*       | ACS evaluation |
|   | & SWA                             | MAJCOM     |                |
| A A A A A A A A A A A A A A A A A A A                     |                                   |            | L GG           |
| Asymptomatic sustained SVT (>10 minutes duration), single | FC I/IA/initial FC II/<br>GBO/SWA | No<br>AETC | ACS review     |
| episode, no ablation†                                     |                                   |            |                |
|   | FC II/III & ATC/GBO               | Maybe      | ACS evaluation |
|   | & SWA                             | MAJCOM     |                |
|   |                                   |            |                |
| Recurrent sustained SVT or any                            | FC I/IA/initial FC                | No‡        | ACS review     |
| degree of SVT associated with                             | II/GBO/ATC/SWA                    | AETC       | 11CB ICVICW    |
| hemodynamic symptoms, no                                  |                                   |            |                |
| ablation  | FC II/III &                       | No‡        | ACS review     |
|   | ATC/GBO/SWA                       | MAJCOM     |                |
| Any degree of SVT requiring                               | FC I/IA/II/III/ &                 | No         | ACS review     |
| antiarrhythmic medication for suppression                 | ATC/GBO/SWA                       | MAJCOM     |                |

<sup>#</sup> Indefinite waiver possible for all asymptomatic, single episodes of SVT of less than 10 beats duration.

If the disease process appears mild and stable, waiver for all classes of flying duties will generally be valid for three years with ACS reevaluation/review at that time for waiver renewal. Each waiver recommendation will specify requirements and timing for waiver renewal.

<sup>\*</sup> Waiver in untrained FC II, III, and RPA individuals is on a case-by-case basis.

<sup>‡</sup> Waiver is possible after successful ablation – refer to "Radiofrequency Ablation (RFA) of Tachyarrhythmias" waiver guide.

A query of AIMWTS in Jan 2018 revealed 398 individuals with waivers including a diagnosis of SVT. The breakdown of the cases is as follows: 21 FC I/IA cases (2 disqualified); 222 FC II cases (23 disqualified); 121 FC III cases (23 disqualified); 5 RPA pilots (0 disqualified); 22 ATC/GBC cases (2 disqualified); and 7 MOD cases (0 disqualified. The majority of the waived cases were for nonsustained single episode of SVT, followed by recurrent non-sustained SVT and then SVT treated with radiofrequency ablation.

## II. Information Required for Waiver Submission.

ACS review/evaluation is required for all classes of flying duties for SVT. One 24-hour Holter monitor should be obtained. If the initial SVT is found on a Holter, then that Holter will suffice and repeat Holter is not warranted unless requested by the ACS/USAF Central ECG Library. If the evaluation reveals only one isolated run of SVT of 3- to10-beats duration, no further testing is typically required. If however, the treating physician deems it clinically necessary to perform any additional studies, it is required that all studies be forwarded to the ACS for review. Aeromedical disposition will be recommended after the studies are forwarded to the ACS for review and confirmation. If more than one run of SVT is present, or if a single run is more than 10-beats in length, ACS evaluation is required. No additional studies are routinely required prior to ACS evaluation. There is no minimum required nonflying observation period for waiver consideration for SVT, unless ablation is performed. Ablation of all SVT mechanisms is addressed in the "Radiofrequency Ablation (RFA) of Tachyarrhythmias" guide.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

For initial waiver (ACS review or evaluation) the AMS should contain the following information:

- A. Complete history and physical examination to include detailed description of symptoms, medications, activity level and CAD risk factors (positive and negative).
- B. Original or legible copy of the tracings documenting SVT (ECG, rhythm strip, Holter, treadmill, etc.). (Notes 1 and 2)
- C. Copy of the report and representative tracings of the Holter, if not provided under B. (Notes 1 and 2)
- D. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. Holter, treadmill, echocardiogram). (Notes 1 and 2)
- E. Additional local cardiac testing is not routinely required but may be requested in individual cases.

For <u>renewal waivers</u> [ACS follow-up evaluations (re-evaluations)] the AMS should contain the following information:

- A. Complete history and physical examination to include detailed description of symptoms, medications and activity level.
- B. Local follow-up cardiac testing is not routinely required prior to ACS re-evaluation. If requested for individual cases, it will have been specified in the report of the previous ACS evaluation.
- C. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. Holter, treadmill, echocardiogram). (Notes 1 and 2)

Note 1: All studies should be submitted electronically to the EKG Library. To expedite the case, recommend sending via FedEx. Include patient's name, SSN and POC at base. The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

Supraventricular tachycardia (SVT) is defined as 3 or more consecutive supraventricular premature beats at a heart rate of 100 beats per minute (bpm) or faster. The term supraventricular usually refers to a narrow QRS complex (<120ms) however there are cases of delayed ventricular activation (referred to as aberrant conduction) that can lead to a widened QRS complex, most often in the setting of a functional or permanent bundle branch block. The two most common forms of pathologic SVT are atrial fibrillation and atrial flutter. These two are covered in a separate waiver guide "Atrial Fibrillation and Atrial Flutter" and will not be discussed in this waiver guide. SVT associated with ventricular pre-excitation with bypass tract is addressed in a separate waiver guide "Wolff-Parkinson-White (WPW) and Other Pre-Excitation Syndromes."

For the remainder of SVTs, the spectrum ranges from an asymptomatic three-beat run that is unnoticed by the individual to a sustained arrhythmia with hemodynamic symptoms such as syncope or very rarely, sudden cardiac death. Approximately 60% of these SVTs are due to a reentry mechanism within the AV node termed an AV node reentrant tachycardia (AVNRT), while 30% of SVTs are associated with a bypass tract. The other 10% of SVTs are a variety of mechanisms, including automatic foci in the atria causing focal atrial tachycardia, multifocal atrial tachycardia and sinus node reentrant tachycardia.<sup>2</sup> Ablation of all SVT mechanisms is addressed in the "Radiofrequency Ablation (RFA) of Tachyarrhythmias" waiver guide. This waiver guide addresses SVT caused by mechanisms other than bypass tracts and includes symptomatic, asymptomatic, sustained (over 30 seconds or with symptoms) and paroxysmal (intermittent with abrupt onset and offset).

In a 1992 Aeromedical Consultation Service (ACS) review of 430 military aviators evaluated for nonsustained or sustained SVT there were no deaths caused by or related to SVT. Forty-two (10%) had symptoms of hemodynamic compromise with syncope, presyncope, light-headedness, chest discomfort, dyspnea or visual changes and an additional 21 (5%) had recurrent sustained SVT without hemodynamic symptoms. Palpitations are not considered to be a hemodynamic symptom. Recurrent is defined as any recurrence, i.e. more than one run of SVT. For this review, sustained SVT was defined aeromedically for the Air Force as SVT lasting greater than 10 minutes. Neither frequent PACs, PAC pairing, nor nonsustained SVT was predictive of hemodynamically symptomatic SVT or of recurrent sustained SVT.<sup>3,4</sup> The study thus documented that most individuals with asymptomatic SVT remained healthy and symptom free for many years. In those with symptomatic SVT, 90% initially presented with these symptoms. The remaining 10% who

later developed symptoms presented with either sustained or recurrent sustained episodes of SVT. Of the multiple factors examined, only presentation with recurrent sustained SVT, hemodynamic symptoms or WPW ECG pattern were at higher risk for future events. Overall, in the above ACS review, of those initially presenting with asymptomatic nonsustained SVT, only 0.9% experienced sustained SVT during the follow-up period, none with associated hemodynamic symptoms. Of those presenting with one or more episodes of sustained SVT, recurrence of sustained SVT was still only 1-2% per year. Civilian population-based studies report recurrence up to 10% per year.<sup>3</sup>

Accepted treatment of acute AVRNT include vagal maneuver, adenosine, or cardioversion. Medications that can be used both acutely and chronically include beta-blocker, non-dihydropyridine calcium channel blockers and/or antiarrhythmics (the latter two are not approved in aircrew). A similar approach is taken for focal atrial tachycardia. For multifocal atrial tachycardia (MAT), most clinicians utilize IV metoprolol or verapamil to treat the acute arrhythmia. For junctional tachycardia, IV beta blockers or IV calcium channel blockers are an appropriate approach to treatment.<sup>5</sup> These interventional approaches are generally safe unless there is a recognized contraindication to use them.<sup>6</sup>

A recent meta-analysis of the efficacy and safety of ablation for the treatment of supraventricular tachycardia shows that this is a safe and effective procedure for our aviators who truly have symptomatic episodes of SVT. There is a greater than 95% success rate with the first ablation treatment for SVT with a rate of adverse events of less than 3%.<sup>7,8</sup>

#### IV. Aeromedical Concerns.

The aeromedical concerns associated with SVT include hemodynamic symptoms associated with any degree of sustained or non-sustained SVT, recurrent episodes of sustained SVT and associated cardiac disease.

Various antiarrhythmic medications may be used clinically to attempt suppression of SVT. Medication concerns include side effect and safety profiles of the medications, proarrhythmic effects and patient compliance in taking the medication every day. Acceptable control with medication is often not achieved with tolerable side effects, and one must accept that the arrhythmia may "break through" and recur on medication. SVT that is otherwise disqualifying would thus still be disqualifying on antiarrhythmic medication. Many antiarrhythmics have a proarrhythmic effect, meaning that they also precipitate tachyarrhythmias, usually ventricular tachyarrhythmias. Given the current high success and low complication rates of ablation, SVT that previously required suppression will now preferentially be referred for ablation.

| ICD-9 code for supraventricular tachycardia |   |  |
|---|---|--|
| 427.0                                       | Paroxysmal supraventricular tachycardia |  |

| ICD-10 code for supraventricular tachycardia |   |  |
|--|---|--|
| I47.1  | Paroxysmal supraventricular tachycardia |  |

#### V. References.

- 1. Link MS. Evaluation and Initial Treatment of Supraventricular Tachycardia. N Engl J Med, 2012; 367: 1438-48.
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- 3. Richardson LA and Celio PV. The Aeromedical Implications of Supraventricular Tachycardia. In The Clinical Basis for Aeromedical Decision Making, AGARD Conference Proceedings 553. Hull (Quebec), Canada, Canada Communication Group, Sep 1994; 25-1 to 25-5.
- 4. Kruyer WB and Davenport ED. Cardiology. Ch. 2 in *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., New York: Castle Connolly Graduate Medical Publishing LTD, 2013.
- 5. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AJA/HRS Guideline for the Management of Adult Patients with Supraventricular Tachycardia. J Am Coll Cardiol, 2016; 67(13): e27-115.
- 6. Al-Khatib SM and Page RL. Acute Treatment of Patients with Supraventricular Tachycardia. JAMA Cardiol, 2016; 1(4): 483-85.
- 7. Spector P, Reynolds MR, Calkins H, et al. Meta-Analysis of Ablation of Atrial Flutter and Supraventricular Tachycardia. Am J Cardiology, 2009; 104: 671-77.
- 8. Helton MR. Diagnosis and Management of Common Types of Supraventricular Tachycardia. Am Fam Physician, 2015; 92(9): 793-800.

### Syncope (Mar 2019)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Edwin Palileo (ACS Cardiologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Restructuring of Waiver Guide, Updated Table 1 and References

#### I. Waiver Consideration

Air Force aviators with recurrent vasodepressor syncope or symptomatic orthostatic hypotension are disqualified for all flying classes. Careful evaluation is necessary before consideration of aeromedical waiver. Waiver consideration is limited to cases in which the risk of recurrence is low and/or the underlying condition or triggering factor can be adequately controlled. Benign syncope limited to predictable settings may be recommended for waiver if there is negligible risk of recurrence in the aviation environment. If a treatable etiology for syncope is found, then correction of the underlying condition may allow a return to flying status. However, certain conditions (e.g., arrhythmia) and/or medications may pose unacceptable risks of recurrence or side effects that could preclude waiver suitability. If the etiology of syncope remains unknown despite extensive diagnostic evaluation, then a clinical judgment based on careful consideration of all available information must be made before allowing a flyer to return to the cockpit. Unexplained or recurrent syncope is disqualifying for retention, and a Medical Evaluation Board is indicated in such cases.

**Table 1: Waiver potential for syncope** 

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation          |
|-------------------|------------------|------------------|-----------------------------------|
| FC I/IA           | Yes              | AETC             | Yes                               |
| FC II/III         | Yes              | MAJCOM           | Yes                               |
| ATC/GBO/SWA       | Yes              | MAJCOM           | At discretion of waiver authority |

## **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

### A. <u>Initial Waiver Request:</u>

1. Complete history and physical exam, including orthostatic blood pressure/pulse readings, cardiovascular exam assessing pulses for rate, rhythm and differences between extremities and auscultation for murmurs or abnormal heart sounds, and neurologic exam assessing mental status, cranial nerves, motor and sensory function, reflexes, plantar reflexes, coordination, gait and Romberg test. The history is the most important component and should include: a complete description of the syncopal episode to include posture, presyncopal symptoms, duration, pre- or post-syncopal amnesia, convulsive accompaniments; any precipitating factors such as venipuncture, medical procedure or standing in formation; other contributory factors (dehydration, inadequate nutrition, strenuous exercise, fatigue, recent illness, etc.) and documentation of any previous syncopal or near-syncopal episodes. Reports from witnesses and first responders are important to obtain and review. A history of

- previous episodes or any other features exceeding the parameters described above, require a waiver. To the extent possible, details of the syncopal episode such as pre-and post-syncopal appearance and behavior, duration of loss of consciousness, post-syncopal posture and any convulsive accompaniments should be based on reliable witness observations. If the episode was unwitnessed, then duration and other details of the syncopal episode cannot be verified.
- 2. If possible, the flight surgeon should interview witnesses personally and the AMS should indicate which elements of the history were provided by witnesses. Past medical history, medications, allergies, and family history (especially of sudden death, arrhythmia or epilepsy) should be documented.
- 3. Reports of consultations and diagnostic testing. Cardiology consultation is required if cardiac etiology is suspected or etiology is unknown. If clinically indicated, tertiary testing such as echocardiogram, Holter or event monitor, tilt-table testing, stress-test, electrophysiology studies, etc. may be necessary. Neurology consultation should be obtained if the LOC cannot be attributed to syncope and/or neurologic deficits are identified or suspected. If clinically indicated, tertiary testing such as neuroimaging or EEGs, etc. may be necessary. Psychology or psychiatry consultation should be obtained if psychogenic factors are suspected. Documentation should include the ECG and results of any laboratory or imaging studies, cardiodiagnostic testing, and neurologic tests such as imaging or EEGs. For cases sent to the ACS for review or evaluation, original images, tapes, etc. will be required. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical and neurologic exam findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Syncope is a common clinical problem, and has been estimated to account for 3-5 percent of emergency room visits and 1 percent of hospital admissions. Any underlying condition that predisposes an aviator to suffer syncopal attacks could lead to incapacitation and loss of aircraft control. For this reason, loss or disturbances of consciousness, symptomatic orthostatic hypotension, or recurrent vasodepressor syncope are all disqualifying. Careful evaluation is required to determine the etiology, risk for recurrence, or long-term complications. Unfortunately, even after thorough evaluation, the cause of syncope remains unknown in many cases. Any aviator being treated with beta blockers, scopolamine, paroxetine, fludrocortisone, or alpha-agonists will not be eligible for a waiver as these medications are not approved for aviation duties in the US Air Force. The evaluation for G-LOC has additional requirements. In-flight G-LOC must be reported as a physiologic event. Evaluation should include a description of the sequence of events and

careful video tape recorder (VTR) review for adequacy of anti-G straining maneuver. Cases in which G-LOC continues to occur despite correction of underlying factors and/or additional and training conducted by an aerospace physiologist are managed IAW AFI 11-4-4, *Centrifuge Training for High-G Aircrew*.

Review of AIMWTS in Jan 2019 revealed a total of 509 waivers submitted with the diagnosis of syncope. Of this total, 61 were FC I/IA (19 disqualified), 158 were FC II (25 disqualified), 21 were RPA pilots (1 disqualified), 200 were FC III (77 disqualified), 46 were ATC/GBC (21 disqualified), and 23 were MOD (4 disqualified). There were a total of 100 disqualifications. Most of the DQ cases were for issues related to syncope – some were on beta blockers, others had unexplained etiologies and others had ongoing issues with syncope. About 20 percent of the DQ cases were disqualified for issues other than syncope.

| ICD-9 code for syncope |                      |  |  |  |  |
|------------------------|----------------------|--|--|--|--|
| 780.2                  | Syncope and collapse |  |  |  |  |

| IC-10 code for syncope |                      |  |  |  |
|------------------------|----------------------|--|--|--|
| R55                    | Syncope and collapse |  |  |  |

### IV. Suggested Readings

1. Benditt D. Syncope in adults: epidemiology, pathogenesis and etiologies. UpToDate, Nov 15, 2018. Link: https://www.uptodate.com/contents/syncope-in-adults-epidemiology-pathogenesis-and-

etiologies?search=syncope&source=search\_result&selectedTitle=5~150&usage\_type=default&disp lay\_rank=5

- 2. Benditt D. Syncope in adults: management. UpToDate, Mar 6, 2019. Link: https://www.uptodate.com/contents/syncope-in-adults-management?search=syncope&source=search\_result&selectedTitle=6~150&usage\_type=default&display\_rank=6
- 3. Benditt D. Syncope in adults: clinical manifestations and diagnostic evaluation. UpToDate, Sep 24, 2018. Link: https://www.uptodate.com/contents/syncope-in-adults-clinical-manifestations-and-diagnostic-

evaluation?search=syncope&source=search\_result&selectedTitle=1~150&usage\_type=default&display\_rank=1

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- 6. Kuriachan V, Sheldon RS, and Platonov M. Evidence-based treatment for vasovagal syncope. Heart Rhythm 2008; 5(11):1609-1614.
- 7. Link MS and Estes M. How to Manage Athletes with Syncope. Cardiol Clin 2007; 25:457-66.

## Systemic Glucocorticoid (Steroid) Therapy (Apr 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

**Significant Changes:** Update to waiver guidance regarding testing of HPA axis function after use of systemic glucocorticoids.

#### I. Waiver Consideration

Active treatment with a systemic glucocorticoid is disqualifying for all aircrew, including ATC and SWA, necessitating DNIF/DNIC. Individuals who are actively being treated with systemic glucocorticoids (GCs) are ineligible for waiver due to the risk of developing aeromedically and operationally significant adverse effects/complications. Treatment with chronic systemic GCs is also disqualifying for GBO duties; however, these members may be considered for waiver if the underlying condition is controlled and the individual is stable on therapy, without idiosyncratic reactions. Of note, the diagnosis of adrenal insufficiency (Addison's disease) is also disqualifying for all aircrew and special duty operators. A waiver for primary adrenal insufficiency is unlikely due to the elevated risk of adrenal crisis.

A history of systemic GC use is not considered disqualifying following discontinuation of the medication, provided that the hypothalamic-pituitary-adrenal (HPA) axis is intact and the underlying condition for which GCs were prescribed is resolved and/or is not disqualifying. Chronic suppression of the HPA axis with systemic GC use can result in adrenal insufficiency and increase the risk of acute adrenal crisis. Therefore, documentation of an intact HPA axis should be accomplished prior to returning any military member to flying or special operational duty if GC use was greater than three consecutive weeks within the last twelve months. If an aeromedical waiver is required for the underlying condition, submit the waiver package after completion of systemic GC treatment and resolution or stabilization of the condition. The aeromedical summary (AMS) should include a recent measurement of the member's basal serum cortisol and if indicated results of an adrenocorticotropic hormone (ACTH) stimulation test (Table 1).

The initial test to determine an intact HPA axis should be a morning serum basal cortisol level while fasting. If serum basal cortisol levels are ≥ 18 mcg/dL, the risk of relative adrenal insufficiency or development of adrenal crisis is low. No further testing is indicated. If the serum basal cortisol level is < 18 mcg/dL, an ACTH stimulation test is used to further assess the HPA axis due to increased risk of underlying adrenal insufficiency. A dose of 250 mcg of Cosyntropin® (recombinant ACTH) is injected IV or IM after a baseline cortisol level is drawn. Stimulated cortisol levels are then drawn at 30 and 60 minutes. A stimulated cortisol level of ≥18 mcg/dL is considered normal. ACTH stimulation testing can be performed at any point after GC discontinuation, but it is typically performed one month after discontinuing therapy. If abnormal, stimulation testing can be repeated at monthly intervals until cortisol levels normalize. Refer to the applicable waiver guide for assistance in the development of an AMS if the underlying condition requires waiver.

Table 1: Workup Required **AFTER** Systemic Glucocorticoid Therapy Discontinuation

| Duration of<br>Glucocorticoid (GC)   | Flying Class and<br>Special Operational | Required Testing   |
|--|---|--|
| Therapy  | Duty <sup>1,2,3</sup>                   |  |
| ≤ 3 weeks of GC therapy, or completion of GC therapy more than 12 months ago                                   | All                                     | N/A  |
| > 3 weeks of GC therapy<br>during the preceding 12<br>months   | All                                     | Serum morning basal cortisol level<br>≥18 mcg/dL – no further testing needed<br><18 mcg/dL – ACTH stim test required |
| > 3 weeks of GC therapy<br>during the preceding 12<br>months <b>and</b> morning<br>cortisol level is <18mcg/dL | All                                     | ACTH stimulation test ≥18 mcg/dL – no further testing needed <18 mcg/dL – Repeat monthly until HPA axis normalizes   |

<sup>1.</sup> Aeromedical waiver is NOT required if systemic GCs have been discontinued, the HPA axis is intact, and there is no underlying disqualifying condition.

## II. Information Required for Waiver Submittal

Not Applicable.

### **III. Aeromedical Concerns**

Hypothalamus-Pituitary-Adrenal (HPA) axis suppression after the completion of GC therapy is a significant aeromedical concern. Individuals with any use of systemic GC therapy are at risk for adrenal insufficiency due to HPA axis suppression; however, this is less likely to occur with a short course of therapy (i.e., less than three weeks duration). The greatest risk of HPA axis suppression occurs when supraphysiologic doses of GCs are administered, duration of therapy is greater than three weeks, split and nighttime doses are administered, or when there is development of Cushingoid features. Tapering GC therapy slowly is required to restore the HPA axis while minimizing the risk of precipitating adrenal insufficiency or crisis in these situations. Adrenal insufficiency presents insidiously with symptoms of fatigue, weight loss, postural dizziness, anorexia, and vague abdominal discomfort. Adrenal crisis presents acutely with symptoms of severe weakness, abdominal pain, nausea, electrolyte derangements, syncope, confusion, and potentially shock. Progressive circulatory collapse can result in death. High emotional or physiologic stress, such as encountered in the aviation and special operation environments, increases the risk of precipitating an acute adrenal crisis. However, this risk remains low in the absence of underlying surgery, infection, or abrupt GC withdrawal. Even without additional risk factors for developing adrenal crisis, all aircrew and special duty operators should undergo testing of the HPA axis after discontinuation of systemic GCs when the course of treatment exceeds three weeks duration within the preceding twelve months. An aeromedical waiver is not required in individuals demonstrating

<sup>2.</sup> Only GBO personnel have waiver potential for chronic systemic GC use once idiosyncratic reactions have been ruled out and the underlying condition is controlled.

<sup>3.</sup> Underlying conditions that are disqualifying per the MSD require waiver submission even if no longer being treated with systemic GCs. Consult the applicable waiver guide if the underlying condition requires waiver.

intact HPA function; however, the underlying condition requiring prolonged GC use may be disqualifying. Underlying conditions that are disqualifying per the MSD require waiver submission. Consult the applicable waiver guide if the underlying condition requires waiver.

## IV. Suggested Readings

- 1. Bornstein S, Allolio B, et al. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism*. 2016; 101(2):364-389.
- 2. Broersen L, Pereira A, Jorgensen J, and Dekkers O. Adrenal Insufficiency in corticosteroids Use: Systematic Review and Meta-Analysis. *Journal of Clinical Endocrinology and Metabolism*. 2015; 100: 2171-2180.
- 3. Joseph R, Hunter A, et al. Systemic glucocorticoid therapy and adrenal insufficiency in adults: a systemic review. *Seminars in Arthritis and Rheumatism*. 2016; 46: 133-141.
- 4. Liu D, Ahmet A and et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy, Asthma and Clinical Immunology*. 2013; 9:30.
- 5. Struja T, Briner, L, et al. Diagnostic accuracy of basal cortisol level to predict adrenal insufficiency in cosyntropin testing: results from an observational cohort study with 804 patients. Endocrine Practice. 2017; 23(8): 949-961.

#### WAIVER GUIDE

Updated: Jun 2016

Supersedes Waiver Guide of Jun 2012

By: Capt Chris McLaughlin (RAM 17) and Dr Dan Van Syoc

Reviewed by Lt Col Timothy Phillips, Urology consultant to AF/SG

### **CONDITION:**

**Testicular Cancer (Jun 2016)** 

### I. Waiver Consideration.

History of testicular cancer is disqualifying for all flying classes. An MEB is required prior to waiver submission. For trained assets, waiver may be submitted after six months in remission and completion of all therapy.

Table 1: Waiver potential for testicular cancer

| Flying Class | Condition         | Waiver Potential | ACS               |
|--------------|-------------------|------------------|-------------------|
| (FC)         |                   | Waiver Authority | review/evaluation |
| I/IA         | Seminoma and      | Yes*             | Yes               |
|              | nonseminoma – all | AETC             |                   |
|              | stages            |                  |                   |
| II/III       | Seminoma and      | Yes+*            | Maybe†            |
| ATC/GBO/SWA  | nonseminoma – all | AFMRA            |                   |
|              | stages            |                  |                   |

<sup>\*</sup>Initial/untrained applicants (all classes) must be in remission 5 years prior to waiver submission

AIMWTS search in Jun 2016 revealed: 119 cases of testicular cancer; 6 FCI/IA, 64 FC II, 43 FC III, 4 GBC and 2 MOD. Of the 119 cases, only ten were disqualified. Of the ten disqualified, six were disqualified because of the diagnosis of testicular cancer (e.g., new metastases to the lung, treated with bleomycin, and recent diagnosis of testicular cancer), one due to complication of the surgery [fracture of coccyx and development of coccydynia, requiring control with narcotics] and three were disqualified for another primary medical condition. The vast majority of the cases were stage I.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the <u>initial waiver</u> for testicular cancer should include the following: A. History – symptoms, pathology, stage, treatment, including date of last treatment, complications of treatment such as pulmonary toxicity, surveillance plan and activity level.

<sup>+</sup> For trained personnel, waiver may be considered six months after treatment completed, in remission and asymptomatic.

<sup>†</sup> For high performance (routine use of aviator mask while flying), individuals treated with bleomycin <u>will no longer</u> require an ACS evaluation unless problems arise and the evaluation is requested by the waiver authority.

- B. Physical genital, lymph nodes, abdomen, chest, and cardiovascular.
- C. Consultation from Urology, Oncology to include all six-month follow-up.
- D. Labs: Initial and latest  $\alpha$ -fetoprotein (AFP),  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG), and lactate dehydrogenase (LDH).
- E. Pulmonary function tests, in individuals who underwent chemotherapy or RT to chest.
- E. Imaging: Chest x-ray and abdominal/pelvic CT.
- F. Pathology report.
- G. Tumor board report.
- H. MEB findings/ALC.

The AMS for <u>waiver renewal</u> for testicular cancer should include the following:

- A. Interval history and detailed physical examination.
- B. All applicable labs and imaging tests as in the initial aeromedical summary.
- C. Consultation from: Urology, Oncology.

#### III. Overview.

Testicular tumors account for 1% the incidence of all tumors and 0.1% of all cancer deaths in men. However, it is the most common malignancy in men in the 15- to 35-year age group. The incidence of testicular cancer in Western Europe and North America has been showing an increase, doubling, in the last 40 years with the etiology unclear. The incidence is 2.5 to 8 times higher in men with cryptorchidism, even when the undescended testis has been brought down surgically. Other risk factors include a personal history of testicular cancer, family history, Caucasian race, and environmental exposures. Testicular cancer most commonly originates from germ cells (95%), but can arise from other cell types (e.g. sex-cord stromal tumors, lymphomas). Germ cell tumors are categorized as seminomas (40%) or non-seminomatous germ cell tumors (NSGCT), which includes embryonal cell carcinoma, yolk sac tumors, choriocarcinomas, and/or teratoma. Germ cell tumors that contain any tumor type in addition to or other than seminoma are categorized as non-seminomatous. This is an important distinction, because the treatment for NSGCT is different than treatment of pure seminoma.

Testicular cancer usually appears as a painless or sometimes (30-40%) painful unilateral intrascrotal mass. Two to three percent of testicular cancers are bilateral, occurring either simultaneously or successively.<sup>2</sup> Five-10% of germ cell tumors present at an extra-gonadal site, predominantly retroperitoneum or mediastinum.<sup>4</sup> These extragonadal germ cell tumors tend to have a delayed presentation, and may manifest with supra-clavicular adenopathy, back pain, lower extremity edema, or symptoms of renal failure from compression of retroperitoneal structures.

Scrotal ultrasound is the gold standard for testicular imaging, having a sensitivity of almost 100% and is used to determine whether a mass is intra- or extra-testicular.<sup>3</sup> However, when a clinical diagnosis indicates a high likelihood of a solid testicular mass, urology referral and treatment should not be delayed by lack of an ultrasound.<sup>2</sup>

Alpha-fetoprotein (AFP),  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG), and lactate dehydrogenase (LDH) (marker of tissue destruction) are serum tumor markers that contribute prognostic value in diagnosis and staging.<sup>2</sup> AFP can be produced by yolk sac tumors, teratoma, embryonal carcinoma or combined tumors but is not increased in pure choriocarcinoma or pure

seminoma.  $\beta$ -hCG is secreted by both seminomas (5-10% - usually below 500 ng/mL) and NSGCT (all choriocarcinomas and 40-60% embryonal carcinoma).<sup>2, 5</sup> Chest x-ray and chest, abdominal and pelvic computed tomography (CT) are also recommended for staging and monitoring.<sup>2</sup>

The standard treatment of all primary testicular cancers is a unilateral radical inguinal orchiectomy with high ligation of the spermatic cord (although testis sparing procedures can be considered in some cases). An inguinal orchiectomy provides not only histopathologic and staging information but potentially a complete cure for individuals with testis-confined

disease.<sup>2,4</sup> In well-defined cases with multiple biopsies of the tumor bed, sparing of the rete testis, normal preoperative plasma testosterone, and tumor size less than 20 mm, the surgeon may choose organ-sparing surgery.<sup>4</sup>

Table 2. American Joint Committee on Cancer (AJCC) Testicular Cancer Staging System.<sup>6</sup>

| Stage | <b>Primary Tumor</b> | Regional Lymph | Distant        | Serum Tumor |  |  |
|-------|----------------------|----------------|----------------|-------------|--|--|
|       | (pT)                 | Nodes (N)      | Metastasis (M) | Markers (S) |  |  |
| 0     | pTis                 | 0              | 0              | 0           |  |  |
| Ι     | pT1-4                | 0              | 0              | 0           |  |  |
| IA    | pT1                  | 0              | 0              | 0           |  |  |
| IB    | pT2, 3 or 4          | 0              | 0              | 0           |  |  |
| IS    | Any pT/Tx            | 0              | 0              | 1-3         |  |  |
| II    | Any pT/Tx            | 1-3            | 0              | X           |  |  |
| IIA   | Any pT/Tx            | 1              | 0              | 0-1         |  |  |
| IIB   | Any pT/Tx            | 2              | 0              | 0-1         |  |  |
| IIC   | Any pT/Tx            | 3              | 0              | 0-1         |  |  |
| III   | Any pT/Tx            | Any N          | 1              | SX          |  |  |
| IIIA  | Any pT/Tx            | Any N          | 1a             | 0-1         |  |  |
| IIIB  | Any pT/Tx            | N1-3           | 0              | 2           |  |  |
|       |                      | Any N          | 1a             | 2           |  |  |
| IIIC  | Any pT/Tx            | N1-3           | 0              | 3           |  |  |
|       |                      | Any N          | 1a             | 3           |  |  |
|       |                      | Any N          | 1b             | Any S       |  |  |

**pT** – pTX (primary tumor cannot be assessed), pT0 (no evidence of primary tumor), pTis (intratubular germ cell neoplasia [carcinoma in situ]), pT1 (tumor limited to testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis), pT2 (tumor limited to testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis), pT3 (tumor invades the spermatic cord with or without vascular/lymphatic invasion, pT4 (tumor invades scrotum with or without vascular/lymphatic invasion).

N-NX (regional lymph nodes cannot be assessed), N0 (no regional lymph node metastasis), N1 (metastasis with lymph node mass 2 cm or less in greatest dimension; or multiple lymph nodes, none more than 2 cm in greatest dimension), N2 (metastasis with lymph node mass > 2 cm but  $\leq 5$  cm in greatest dimension; or multiple lymph nodes, any one mass > 2 cm but  $\leq 5$  cm greatest diameter), N3 (metastasis with lymph node mass > 5 cm in greatest dimension).

 $\mathbf{M}-\mathbf{M}\mathbf{X}$  (distant metastasis cannot be assessed), M0 (no distant metastasis), M1 (distant metastasis), M1a (non-regional nodal or pulmonary metastasis), M1b (distant metastasis other than to non-regional lymph nodes and lungs).

S – SX (marker studies not available or not performed), S0 (marker study levels within normal limits), S1 (LDH <1.5 times upper limit of normal and hCG < 5000[mIu/ml] and AFP < 1000 [ng/ml]), S2 (LDH 1.5 to 10 times upper limit of normal or hCG 5000-50,000 or AFP 1000-10,000), S3 (LDH > 10 times normal or hCG > 50,000 or AFP > 10,000).

Approximately 80% of seminomas present with stage I disease (limited to the testis), while 15% have stage II disease. NSGCT has a greater tendency to present with metastatic disease. Seminomas most commonly metastasize via lymphatics to retroperitoneal nodes, and more rarely spread hematogenously to other areas (e.g., liver, lung, bones, or brain). Seminomas are very sensitive to radiation therapy (RT) while NSGCT are more radioresistant. Seminomas frequently do not have elevated tumor markers, while NSGCT have elevated  $\beta$ -hCG or AFP in 85% of cases. A, 7

Most patients with Stage I seminoma are cured by orchiectomy alone. A small percentage of patient relapse. To prevent relapse in patients with stages IA and IB pure seminoma, the standard management options after initial orchiectomy include active surveillance, RT, or chemotherapy with 1-2 cycles of carboplatin. The disease specific survival for stage I disease is 99% irrespective of the management strategy used. With respect to surveillance, a number of prospective non-randomized studies of surveillance have been conducted. The relapse rate seen in these studies is 15-20% at 5 years, and most of the relapses are first detected in infra-diaphragmatic lymph nodes. Surveillance is listed as the preferred option (category 1) for patients with pT1-pT3 tumors by the NCCN Testicular Cancer Panel. If surveillance is not applicable, alternatives are either adjuvant carboplatin or RT. Each has distinct advantages and disadvantages.

When RT is elected, acute side effects are mostly gastrointestinal, particularly nausea. <sup>12</sup> One-2 cycles of single agent carboplatin has similar survival rates to radiotherapy. <sup>13</sup> The benefits of adjuvant treatments must be balanced with the long-term risks of side effects (heart disease and secondary malignancy for RT / long-term effects of carboplatin remain undetermined). Individuals with stage II seminomas treated with post orchiectomy RT have 5-year disease-free survival rates of approximately 80%, ranging from 70 to 92%, but overall survival with salvage therapy approaches 100%. <sup>2,4,7</sup> In individuals with distant metastases or bulky retroperitoneal disease after orchiectomy (e.g., stage IIC, III) chemotherapy is the most common treatment, most commonly bleomycin, etoposide and cisplatin (BEP). More than 90% of individuals with stage III achieve complete response.

In contrast to patients with pure seminoma, those with NSGCT are more likely to harbor metastatic disease at presentation. Approximately 33% of individuals with NSGCT present with disease limited to the testis (stage I). NSGCT treatment after orchiectomy depends on stage at presentation, and can include observation, chemotherapy or retroperitoneal lymph node dissection (RPLND), individually or in combination. Treatment planning is based on tumor markers and their behavior after orchiectomy, radiographic staging with CT, and risk stratification. Occult metastatic disease is frequent, with 30% of clinical stage I NSGCT having pathologic evidence of metastatic disease (stage II or greater) despite normalization of tumor markers and normal imaging.<sup>7, 14</sup> Metastasis is most commonly found in the retroperitoneal lymph nodes, but can skip the retroperitoneum, with pulmonary lesions being the next most common site. RPNLD is the only modality that can accurately delineate pathologic stage I from pathologic stage II. The risk of relapse in observation of stage I NSGCT is 27-35%, with more than 50% during the first year after orchiectomy, although

late relapses (≥ 24 months) occurring in 10%.<sup>1,4</sup> The cure rate for clinical stage I is approximately 95%, with similar rates regardless of treatment (observation + salvage therapy if recurrence develops, primary RPNLD, or primary chemotherapy). However, it should be noted that salvage therapy is almost always more intensive and complex than primary RPLND or primary chemotherapy. For higher stage NSGCT, chemotherapy is usually the initial treatment, followed by post-chemo RPLND or surveillance.<sup>2</sup> The most common chemotherapy for NSGCT is a combination of bleomycin, etoposide and cisplatin. However, similar cancer control rates have been achieved with elimination of bleomycin and a longer course of therapy with etoposide and cisplatin in an effort to avoid the pulmonary toxicity of bleomycin.

Individuals with seminomas with stage I, II and stage IIIA and IIIB and individuals with NSGCT with stage I, II and IIIA have a five-year survival of 91%.<sup>4, 15</sup> Stage IIIC seminomas or stage IIIB NSGCT have a five-year survival rate of 79%. Stage IIIC NSGCT have a five-year survival rate of 48%.<sup>15</sup>

There are some potential long-term toxicities of chemotherapy. <sup>14</sup> These possible long-term side effects include the following:

- 1. Leukemia: there is a 0.5-2% risk of developing leukemia after treatment with etoposide, depending on the total dose administered.
- 2. Other solid tumors: there is an approximately 1.5-fold increased risk for second malignancies after chemotherapy for testis cancer.
- 3. Pulmonary toxicity: there is a 2-3% risk for pulmonary fibrosis after treatment with bleomycin, depending on total dose. Rarely, this can be fatal. Bleomycin also increases the risk of pneumonitis associated with exposure to high concentrations of oxygen. Individuals treated with bleomycin should avoid prolonged exposure to high concentrations of oxygen. Development of pulmonary toxicity can be measured with pulmonary function testing with diffusion capacity testing (DLCO) and bleomycin therapy can be curtailed in this event.
- 4. Vascular toxicity: up to 1/3 of patients can develop Raynaud's phenomenon after chemotherapy. Patients may need to protect their hands with gloves while working in a cold environment if this develops. There is a 2-2.5-fold increased risk of myocardial infarction after chemotherapy. Patients should protect their cardiovascular health by refraining from tobacco use and maintaining a healthy lifestyle and diet.
- 5. Neurotoxicity: peripheral sensory neuropathy, which can include ototoxicity, is associated with cisplatin therapy. In general, it is mild and not functionally limiting and frequently improves with time. If it occurs, it usually manifests as paresthesia or dysesthesia in the extremities and does not limit activity. Motor neuropathy is extremely rare.
- 6. Nephrotoxicity: cisplatin is also associated with nephrotoxicity. Periodic assessment of renal function should be included in the follow up regimen.
- 7. Infertility: the BEP chemotherapy regimen will cause infertility in all patients temporarily. There is a 25% chance that sperm production will never recover. There is a 50% chance that sperm production will recover to pre-treatment levels. This generally occurs between 12 and 36 months after completion of therapy.<sup>14</sup>

Semen cryopreservation should be discussed with men diagnosed with testicular cancer prior to instituting therapy, as treatment may have an irreversible impact on fertility.

#### IV. Aeromedical Concerns.

The aeromedical concerns primarily relate to surveillance after diagnosis and the potential long-term morbidity of chemotherapy. Surveillance is intensive and mandatory, regardless of the initial treatment (observation, radiotherapy, chemotherapy, RPLND). Assignments and assignment limitations should be instituted in order to comply with follow up recommendations. Follow up should be scheduled in accordance with standards published by the National Comprehensive Cancer Network at <a href="www.NCCN.org">www.NCCN.org</a>. Follow up depends on tumor type, stage and initial treatment. The NCCN is a non-profit consortium of cancer treatment centers that provides evidence-based guidelines for the management and follow up of cancers and should be considered a standard of care in the management and follow up of testicular cancer. 

[16]

Chemotherapeutic morbidity, particularly pulmonary toxicity associated with bleomycin, must be ruled out in the flying community. In the past, the use of bleomycin in aviators would have been permanently disqualifying. This was based on the risk of pulmonary fibrosis with exposure to oxygen. The value of bleomycin in the treatment of malignancies is in part a function of its specific toxicity, since it does not induce bone marrow aplasia, and thus does not add to the toxicity that limits most oncologic drugs. Instead, the principal target organ of bleomycin-induced injury is the lung, with acute pulmonary damage occurring in 6-18% of treated patients. The pathophysiology of delayed toxicity of bleomycin is complex. In the medical literature of the last thirty years, a number of patients have been described who, having previously received bleomycin therapy, have developed pulmonary toxicity when undergoing subsequent surgery. Typically, these have been young individuals receiving modest levels of oxygen (33-42%) during long operations (4-8 hours). The true incidence of such delayed toxicity is unknown, since the subsequent literature has largely consisted of isolated case reports or small series. <sup>17, 18</sup> A more cogent argument can be made that the period of risk is primarily in the first year after therapy, since most cases occurred within that time frame. However, it is equally possible that this observation represents a bias related to the timing of operative intervention.

Applicable data had been non-existent, a state of affairs that has been somewhat altered by unpublished data recently supplied by the Duke Hyperbaric Unit.<sup>17</sup> Although it had been the practice in hyperbaric medicine to avoid hyperoxia in bleomycin-treated individuals, the undoubted benefit from hyperbaric oxygen (HBO) in wound healing and osteonecrosis posed against the uncertain risk of delayed bleomycin toxicity led several years ago to a change in policy. Since then, the Duke unit has treated 11 individuals previously exposed to bleomycin with HBO. There was a wide range of time between the last dose of bleomycin and the institution of HBO, ranging from 1 month to 22 years. The range of cumulative bleomycin doses was not noted. Anywhere from 8 to 44 treatments with 100% oxygen at 2 ATA (PiO2 ~ 1475 mmHg) were administered for two hours per treatment, once or twice daily. One individual experienced significant chest discomfort and a decline in diffusion capacity of 50%; both resolved following a break in treatment, and she successfully completed HBO treatment with a reduction in frequency of her sessions. More recently, researchers at Duke described 15 patients with bleomycin exposure prior to HBO and without any adverse changes in arterial blood gases, spirometry, chest radiographs, or clinical symptoms. 19 While the Duke experiences do not represent occupational exposure per se, and the number of individuals treated is small, the amount of oxygen exposure from HBO therapy is far in excess of what would be expected in aviation, and suggests that the risk of delayed toxicity outside the operating room may be minimal.

Based on this data, policy was changed for aviators treated with bleomycin. Those aviators returning to non-high performance aircraft would be evaluated as usual, addressing risks of tumor recurrence and potential toxicity from chemotherapy. Assuming they had not developed bleomycin pneumonitis during therapy, then no restrictions from altitude chamber or other sporadic oxygen exposure is warranted. For aviators returning to a high-performance cockpit (aircraft requiring routine use of 100% oxygen), and assuming that bleomycin pneumonitis had not occurred during their treatment protocol, an ACS evaluation is no longer required. For those who did experience bleomycin pneumonitis, the ACS evaluation will include pulmonary function testing (spirometry, plethysmographic lung volumes, and diffusion capacity) and high-resolution CT scanning of the lungs. This evaluation will be repeated at the one and two year point of active flying. Because it is possible, and biologically plausible, that the common perception of an increased period of risk within the first year is correct, a grounding period of one year from the end of treatment is required before the baseline evaluation is undertaken.

There have been case reports of life-threatening pneumonitis developing in patients with a history of bleomycin-induced lung injury, who were later given supplemental oxygen for surgical procedures. Therefore, aviators who have a history of bleomycin-induced lung injury should not be allowed to return to airframes that require routine use of 100% oxygen. Also, they should be exempted from the portions of the altitude chamber qualification that require 100% oxygen use. Use of 100% oxygen during emergencies such as fire or rapid decompression is acceptable and should not be discouraged. <sup>17, 18</sup>

| ICD-9 code for testicular cancer |   |  |  |
|----------------------------------|---|--|--|
| 186.9                            | Malignant neoplasm of testis, other and unspecified |  |  |

| ICD-10 code for testicular cancer |   |  |  |  |
|-----------------------------------|---|--|--|--|
| C62.90                            | Malignant neoplasm of unspecified testis, unspecified |  |  |  |
|                                   | whether descended or undescended                      |  |  |  |

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### WAIVER GUIDE

Updated: Jul 2015

Supersedes Waiver Guide of Oct 2011

By: Lt Col Tory Woodard (RAM 16) and Dr Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

### **CONDITION:**

Thalassemia (Jul 2015)

### I. Waiver Considerations.

Hemoglobinopathies and thalassemia are disqualifying for flying classes I/IA, II, III, and SWA duties. Thalassemia is not specifically disqualifying for ATC/GBO duties. USAF experience suggests a waiver for  $\alpha$ - and  $\beta$ -thalassemia minor/trait is likely as long as the anemia is minimal and the individual is symptom free. For the purposes of this discussion, anemia shall be considered minimal if hematocrit levels remain above 40 for men and 35 for females. Any anemia is disqualifying for retention and all flying class, ATC and SWA duties when symptomatic, or when response to therapy is unsatisfactory, or when therapy requires more than annual hematologist follow-up. Due to limited USAF experience and the <u>potential clinical variations</u> between individuals, heterozygous thalassemia associated with other hemoglobinopathies cannot be generalized and waiver status for these circumstances will be considered on a case-by-case basis.

Table 1: Waiver potential for various types of thalassemia.

| Flying Class         | Condition                          | Waiver Potential  |
|----------------------|------------------------------------|-------------------|
|                      |                                    | Waiver Authority  |
| I/IA                 | α-thalassemia (silent thalassemia) | Yes* <sup>†</sup> |
|                      | and $\alpha$ -thalassemia trait    | AETC              |
|                      | Hb H disease                       | No                |
|                      |                                    | AETC              |
|                      | β-thalassemia minor                | Yes* <sup>†</sup> |
|                      |                                    | AETC              |
|                      | β-thalassemia intermedia and major | No                |
|                      | p manager                          | AETC              |
| II/III/SWA#          | α-thalassemia (silent thalassemia) | Yes*†             |
|                      | and $\alpha$ -thalassemia trait    | MAJCOM            |
|                      | Hb H disease                       | No                |
|                      |                                    | MAJCOM            |
|                      | β-thalassemia minor                | Yes*†             |
|                      | F                                  | MAJCOM            |
|                      | β-thalassemia intermedia and major | No                |
|                      | F                                  | MAJCOM            |
| ATC <sup>&amp;</sup> | N/A                                | N/A               |
| GBO!                 | N/A                                | N/A               |

<sup>\*</sup> Waiver likely if asymptomatic and hematocrit >32.

Review of AIMWTS in May 2015 revealed 176 cases with a diagnosis of thalassemia or thalassemia trait. Breakdown of the cases revealed: 43 FC I/IA (4 disqualified), 41 FC II (3 disqualified), 65 FC III (4 disqualified), 26 ATC/GBC (1 disqualified), and 1 MOD (0 disqualified). Many of these cases were granted an indefinite waiver. Of the 12 disqualified cases, most were disqualified for reasons other than the thalassemia.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition have been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations. If required, MEBs should be completed prior to waiver submission.

<sup>†</sup> Indefinite waiver likely if stable hematocrit > 38 for males and >36 for females and asymptomatic.

<sup>#</sup> Initial FC II/III waiver authority is AETC.

<sup>&</sup>amp; Thalassemia is not specifically disqualifying for ATC duties. However, anemia associated with thalassemia may be disqualifying when symptomatic, or when response to therapy is unsatisfactory, or when therapy requires more than annual hematologist follow-up; in that case AFMRA is initial waiver authority

<sup>!</sup> Thalassemia is not specifically disqualifying for GBO duties. Anemia is also not specifically disqualifying for GBO duties, but the underlying etiology (other than thalassemia) may still require aeromedical waiver.

The aeromedical summary for an <u>initial waiver</u> should include the following:

- A. History symptoms (including pertinent negatives) such as fatigue, headache, shortness of breath, dizziness, palpitations and activity level. Additionally, ethnicity, place of ancestral origin, and family history of "anemia" should be included.
- B. Physical Exam to include skin, mucous membranes, heart, lung, abdomen (including presence or absence of palpable spleen) and extremities.
- C. CBC with reticulocyte count.
- D. Iron studies (serum iron, total iron binding capacity (TIBC), and serum ferritin).
- E. If spleen is palpable, abdominal ultrasound to quantify splenomegaly.
- F. Hemoglobin electrophoresis.
- G. Blood smear results (looking for number of target cells, dacrocytes, etc.)
- H. Hematology consult.

The aeromedical summary for waiver renewal should include the following:

- A. History Brief summary of symptoms or results that led to diagnosis, or any new symptoms (include pertinent negatives).
- B. Physical skin, mucous membranes, heart, lung, abdomen, extremities.
- C. CBC annually.
- D. Iron studies.

#### III. Overview.

Thalassemia refers to a spectrum of disorders that result from reduced or absent globin chain production. Typically an autosomal recessive condition, it is among the most common genetic disorders worldwide. Although rare in the United States, an estimated 5% of the world's population may be affected.<sup>1, 2</sup> Highest thalassemia gene frequencies occur in areas surrounding the Mediterranean, and in South Asia, South-East Asia, and Oceania, and is thought to have developed due to the protective effects against malaria in heterozygotes.<sup>3</sup> About 15% of American Blacks are silent carriers for α-thalassemia. α-thalassemia trait (minor) occurs in 3% of American Blacks and also in 1-15% of persons of Mediterranean origin. β-thalassemia has an incidence of 0.8% in American blacks and 10-15% in individuals from the Mediterranean and Southeast Asia.<sup>4</sup> Over 50% of the US thalassemia population now consists of people of Asian ancestry due to demographic changes from immigration and other population shifts.<sup>5</sup>

# Figure 1. Thalassemia Syndromes<sup>6,7</sup>

- Alpha-thalassemia
  - O Silent α-thalassemia
  - $\circ$   $\alpha$ -thalassemia trait ( $\alpha^0$  or  $\alpha^+$ )
  - Hb H disease
  - o Hb Bart's Hydrops Fetalis
- Beta-Thalassemia
  - o Thalassemia minor (trait)
  - o Thalassemia intermedia
  - o Thalassemia major
- Others
  - o Delta-beta Thalassemia (Hb Lepore)

- Variant hemoglobin with thalassemia phenotype (Hb E)
- o Beta-Thalassemia with other variant hemoglobin (Hb S, Hb C, Hb E)

The thalassemias are characterized by reduction in the synthesis of globin chains ( $\alpha$  or  $\beta$ ) causing decreased hemoglobin synthesis and a hypochromic microcytic anemia from defective hemoglobinization of red blood cells.<sup>8</sup> Clinical severity varies widely, depending on the degree of impaired or altered synthesis and whether coinheritance of other abnormal globin alleles exists.<sup>4</sup> Severity may range anywhere from a silent carrier state through severe hemolytic anemia, or even fetal demise.<sup>1</sup>

Recall normal circulating adult hemoglobin is approximately 98% hemoglobin A. It is a tetramer containing two  $\alpha$  chains and two  $\beta$  chains ( $\alpha_2\beta_2$ ). Hemoglobin A<sub>2</sub> normally comprises 1-2% of adult hemoglobin and is formed of two  $\alpha$  chains and two  $\delta$  (delta) chains ( $\alpha_2\delta_2$ ). Hemoglobin F is the major fetal hemoglobin, but comprises less than 1% of adult hemoglobin. It is formed of two  $\alpha$  chains and two  $\gamma$  (gamma) chains ( $\alpha_2\gamma_2$ ).

#### α-Thalassemia

 $\alpha$ -thalassemia (Figure 2 and Table 1) results from deletion of one or more of the four genes responsible for  $\alpha$ -globin synthesis. Four-gene deletions result in fatal hydrops fetalis with 90-95% Hb Barts ( $\gamma_4$ ). Three-gene deletions results in hemoglobin H (Hb H). A two-gene deletion results in individuals with  $\alpha$ -thalassemia trait, and a one-gene deletion results in the "silent" carrier state. <sup>10</sup>

## Figure 2: α-Thalassemia Terminology<sup>6</sup>

- - $\alpha/\alpha\alpha$  heterozygous  $\alpha^+$ -thalassemia (silent  $\alpha$ -thalassemia)
- $-\alpha/-\alpha$  homozygous  $\alpha^+$ -thalassemia ( $\alpha^+$ -thalassemia trait)

### $\alpha^0$ -thalassemia

- --/ $\alpha\alpha$  heterozygous  $\alpha^0$ -thalassemia ( $\alpha^0$ -thalassemia trait)
- --/-- homozygous α<sup>0</sup>-thalassemia (Hb Bart's)

# Compound heterozygous $\alpha$ -thalassemia

--/- $\alpha$  heterozygous  $\alpha^0$  with heterozygous  $\alpha^+$  (Hb H)

<u>Key</u>:  $\alpha\alpha/\alpha\alpha$  = normal individual (2  $\alpha$ -globin genes on each of two chromosomes)

-  $\alpha$  = one gene on a chromosome

- - = no genes on a chromosome

Individuals with  $\alpha$ -thalassemia trait may not be anemic, but may exhibit mild hypochromia and microcytosis with laboratory exam. Their Hb  $A_2$  and Hb F levels are normal. Hb H disease results in hemolytic anemia with ineffective erythropoiesis, although survival into mid-adult life without transfusions is now common. Hb Bart's is a more virulent condition, with the resulting hydrops fetalis producing death in-utero or shortly after birth.<sup>4</sup> Readily available gap PCR gene deletion testing can identify the majority of persons with  $\alpha$ -thalassemia, including silent  $\alpha$ -thalassemia (- $\alpha/\alpha\alpha$ ).<sup>10</sup>

Table 2: α-Thalassemia Hemoglobins and Red Blood Cell Indices<sup>11</sup>

| Phenotype                         | Genotype | HbA<br>(%) | HbA <sub>2</sub><br>(%) | HbF<br>(%) | н <b>рн</b><br>(%) | HbBart<br>(%) | Hb<br>(g/dL) | MCV<br>(fl) | MCH<br>(pg) |
|-----------------------------------|----------|------------|-------------------------|------------|--------------------|---------------|--------------|-------------|-------------|
| Normal                            | αα/αα    | 96-98      | 2-3                     | <1         | 0                  | 0             | 15           | 90          | 30          |
| Silent                            | - α/αα   | 96-98      | 2-3                     | <1.0       | 0                  | 0             | 14.5         | 75-85       | 26          |
| Trait                             | /αα or   | 96-98      | 1.5-3.0                 | <1.0       | 0                  | 0             | 12-13        | 68-76       | 23          |
| $(\alpha^0 \text{ or } \alpha^+)$ | - α/-α   |            |                         |            |                    |               |              |             |             |
| Compound                          | /-α      | 60-90      | <2.0                    | <1.0       | 0.8-40             | 2-5           | 7-10         | 57-65       | 18          |
| Bart's                            | /        | 0          | 0                       | 0          | 5-10               | 85-90         | 3-8          | 136         | 32          |

## **β-Thalassemia**

β-thalassemia (see Table 2) is usually caused by one of more than 200 point mutations in β-globin chain synthesis, or may rarely result from deletions.<sup>6</sup> Homozygous β-thalassemia is a serious medical condition. Previously, most persons with the condition died in childhood, but individuals treated from birth with transfusions now commonly live to over forty years of age.<sup>7</sup> β-Thalassemia major, with either absent or reduced beta chain production, results in a significant amount of HbF  $(\alpha_2 \gamma_2)$ . This tetramer is unstable, readily breaks down, and thus results in severe microcytic, hypochromic anemia. It may be associated with massive enlargement of the liver and spleen, due to excessive red-cell destruction and extramedullary erythropoiesis. Pathological fractures may result from thinning of the cortex secondary to bone marrow expansion. 12 Transfusion therapy is necessary to sustain life.<sup>7</sup> β-thalassemia intermedia encompasses a wide range of disorders between transfusion-dependent patients with growth and development retardation to asymptomatic patients.<sup>6</sup> Thalassemia minor (thalassemia trait) usually presents as only minimal or mild anemia, but may demonstrate profound microcytosis, hypochromia, and target cell presence. Hemoglobin electrophoresis classically reveals an elevated HbA2, but some forms are associated with normal HbA<sub>2</sub> and/or elevated HbF. Individuals with β-thalassemia trait should be warned that their blood picture resembles iron deficiency and can be misdiagnosed.<sup>4</sup>

Table 3: β-Thalassemia Hemoglobins and Red Blood Cell Indices.<sup>8</sup>

| Phenotype       | β-Globin<br>Genes                                | HbA<br>(%) | HbA <sub>2</sub><br>(%) | HbF<br>(%) | Hb (g/dL)         | MCV<br>(fl) | MCH<br>(pg) |
|-----------------|--|------------|-------------------------|------------|-------------------|-------------|-------------|
| Normal          | Homozygous β                                     | 97-99      | 1-3                     | <1         | 15                | 90          | 30          |
| β minor (trait) | Heterozygous<br>β <sup>0</sup> or β <sup>+</sup> | 80-95      | 4-8                     | 1-5        | ♂ 11-15<br>♀ 9-14 | <79         | <27         |
| β intermedia    | *  | 10-30      | 2-5                     | 70-90      | 7-10              | 50-80       | 16-24       |
| β major         | Homozygous $\beta^+$ or $\beta^0$                | 0-10       | 4-10                    | 90-96      | <7                | 50-70       | 12-20       |

\*Homozygous  $\beta^+$  (mild) or compound heterozygous  $\beta^+/\beta^0$  (more severe)

## **Other Thalassemias**

<u>Delta-beta</u> ( $\delta\beta$ ) thalassemia produces a phenotype of  $\beta$  –thalassemia intermedia when homozygous and a  $\beta$ -thalassemia minor phenotype when heterozygous. It does not demonstrate increased Hb A<sub>2</sub>

 $(A_2 \text{ may usually be } < 4\%)$ . When a person with microcytic, hypochromic anemia is noted to have Hb  $A_2$  levels less than 4% and elevated HbF levels,  $\delta\beta$ - thalassemia should be suspected. The Kleihauer-Betke (K-B) acid elution test may be used to distinguish it from hereditary persistence of fetal hemoglobin (HPFH).

Sickle cell trait (Hb AS)/ $\beta$ -thalassemia, may produce a symptomatic clinical sickling syndrome similar to Sickle Cell Anemia (Hb SS) disease, unlike Sickle cell trait without thalassemia. Hemoglobin Lepore produces a thalassemia syndrome varying in severity from  $\beta$ -thalassemia intermedia to  $\beta$ -thalassemia major when homozygous. The heterozygous condition is clinically comparable to  $\beta$ -thalassemia minor, but the hemoglobin electrophoresis shows Hb Lepore, mildly increased Hb F, and low Hb  $A_2$ .

Hb E has increasing prevalence worldwide with frequencies as high as 80% in some populations in South and Southeast Asia. It has now become the most common thalassemia syndrome on the U.S. West Coast. Heterozygous Hb E or Hb E trait (Hb AE) or Hb E/ $\alpha^0$ -thalassemias cause mild anemia with normal indices. They are otherwise asymptomatic. Hb E/ $\alpha^+$ -thalassemia or homozygous Hb E produce hypochromic microcytic anemia and may occasionally cause splenomegaly. Hb E/ $\beta^0$  is associated with splenomegaly and causes clinical illness similar to β –thalassemia intermedia or major. It is occasionally mild enough to be found incidentally in adulthood. 13, 14

Hb C is another significant variant hemoglobin thalassemia. Heterozygous Hb C trait is asymptomatic and may have no anemia or red blood cell changes. Hb C/β-thalassemia, however, causes a clinical syndrome with microcytic anemia and occasional splenomegaly. The severity is usually mild and the clinical findings depend on whether the  $\beta^0$  or  $\beta^+$ -thalassemia form is involved.<sup>7, 15, 16</sup>

#### IV. Aeromedical Concerns.

The diagnosis of thalassemia syndrome for aeromedical purposes does not require the detailed genotypic analysis that may be necessary for genetic counseling. Flyers diagnosed with these syndromes should be informed that formal genetic counseling with their partner is recommended, due to the potentially catastrophic outcomes in their offspring. Further testing may be required for genetic counseling purposes in these cases. In general,  $\beta$ -thalassemia and variant hemoglobins can be diagnosed utilizing hemoglobin electrophoresis.  $\alpha$ -thalassemia was often a diagnosis of exclusion, because no readily available direct testing existed for this condition. While most cases of  $\alpha$ -thalassemia can now be easily classified by PCR deletion analysis, a presumptive diagnosis based on clinical phenotype evaluation may be more cost effective and adequately sufficient for aeromedical disposition.  $^{6, 11, 17}$ 

The primary aeromedical concern regarding the thalassemia syndromes include anemia, hemolysis, splenomegaly, and sickling potential. Although unlikely, mild cases of homozygous thalassemia syndromes could present for aeromedical disposition. Thalassemias may compromise the oxygen-carrying capacity of the individual when significant anemia exists or sickling symptoms occur. Flying duties are thus typically contraindicated for  $\beta$ -thalassemias major and intermedia, Hb AS/ $\beta$ -thalassemia, Hb AE/ $\beta$ -thalassemia, Hb H, and other similar conditions. Splenomegaly is disqualifying for many USAF flying classes and may have service retention implications if unable to be surgically corrected.

Heterozygous  $\beta$ -thalassemias generally do not impair normal life and are compatible with aircrew duties. The potential concern is the severity of the anemia and the possibility of splenomegaly. Most individuals with  $\beta$ -thalassemia minor require no medication and live normal lives, suffering no ill effects or restrictions. Heterozygous  $\alpha$ -thalassemias, such as silent thalassemia and  $\alpha$ -thalassemia trait, rarely produce more than a mild anemia and are therefore compatible with most flying duties.

## Table 4. Suggested Diagnostic Testing<sup>6, 11</sup>

- 1. CBC with peripheral smear and reticulocyte count
- 2. Iron studies (serum iron, iron saturation/TIBC and ferritin)
- 3. Hemoglobin electrophoresis (including Hb H and Hb Bart analysis)

| Hemoglobin Electrophoresis Results       | Suspected Diagnosis                     |
|--|---|
| Normal hemoglobin types                  | Presumed α-thalassemia                  |
| Normal Hb A <sub>2</sub> and Hb F levels |   |
| No iron deficiency                       |   |
|  |   |
| Elevated Hb A <sub>2</sub>               | β-thalassemia                           |
| Elevated or normal Hb F                  |   |
| No variant Hb                            |   |
| Hb A <sub>2</sub> <4% with elevated Hb F | Suspect δβ-thalassemia, even if no      |
|  | Hb Lepore found.                        |
|  | Kleihauer-Betke (K-B) acid elution test |
|  | may be used to distinguish HPFH.        |
| Hemoglobin variant                       | Hb C, Hb E, Hb S                        |
|  | (Heterozygote vs. Homozygote)           |
| Hemoglobin variant                       | Combination variant hemoglobin          |
| With elevated Hb A <sub>2</sub> , Hb F   | β-thalassemia                           |

| ICD-9 codes for thalassemia |  |  |
|-----------------------------|--|--|
| 282.4                       | Thalassemia  |  |
| 282.7                       | Other hemoglobinopathies                           |  |
| 282.8                       | 282.8 Other specified hereditary hemolytic anemias |  |
| 282.9                       | Hereditary hemolytic anemia, unspecified           |  |

| ICD-10 codes for thalassemia |  |  |
|------------------------------|--|--|
| D56.9                        | Thalassemia, unspecified                           |  |
| D58.2                        | Other hemoglobinopathies                           |  |
| D58.8                        | D58.8 Other specified hereditary hemolytic anemias |  |
| D58.9                        | Hereditary hemolytic anemia, unspecified           |  |

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#### WAIVER GUIDE

Updated: Aug 2015

Supersedes Waiver Guide of Dec 2011

By: Dr Kevin Van Valkenburg (RAM 16) and Dr. Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

#### **CONDITION:**

Thrombocytopenia, Idiopathic Thrombocytopenic Purpura (ITP), & Idiopathic Thrombotic Thrombocytopenic Purpura (TTP) (Aug 2015)

#### I. Waiver Consideration.

Platelet dysfunctions, idiopathic thrombocytopenia, and generally platelet counts less than 100 X 10<sup>9</sup>/L are disqualifying for all flying, special duty positions, and retention. As such, any persistent or symptomatic condition leading to a decreased platelet count is disqualifying. Thrombocytopenia of any cause that requires prolonged therapy, intense medical supervision, or has an unsatisfactory response to therapy would be disqualifying and result in the need for a waiver.

Table 1: Waiver potential for thrombocytopenia, ITP, or TTP

| Flying Class (FC) | Condition                                 | Waiver Potential |
|-------------------|---|------------------|
|                   |   | Waiver Authority |
| I/IA              | Thrombocytopenia or ITP                   | Yes              |
| Initial II/III    | (childhood, < 18-years-old)               | AETC             |
|                   | that resolved.                            |                  |
|                   |   |                  |
|                   | ITP/TTP/causes other than                 | No               |
|                   | transient (≥18-years-old).                | AETC             |
| II//III           | Single episode of ITP                     | Yes              |
| ATC/GBO/SWA       | resolved with platelets >100              | MAJCOM           |
|                   | $X 10^9/L.*$                              |                  |
|                   |   | Yes              |
|                   | Recurrent ITP or not                      | AFMRA            |
|                   | resolved with platelets                   |                  |
|                   | maintained at >50 X 10 <sup>9</sup> /L    |                  |
|                   | and <100 X 10 <sup>9</sup> /L.*           |                  |
|                   |   | No               |
|                   | Recurrent or not resolved                 | AFMRA            |
|                   | ITP with platelets                        |                  |
|                   | maintained at $<50 \times 10^9/L$ .       |                  |
|                   |   | Yes              |
|                   | TTP resolved with platelets               | AFMSA            |
|                   | $>100 \text{ X } 10^9/\text{L}^{\dagger}$ |                  |
|                   |   | No               |
|                   | Recurrent TTP                             | AFMRA            |

<sup>\*</sup> Off all treatment and 6 months of stable platelets.

<sup>†</sup> Waiver not considered until two years after resolution and ACS evaluation is likely.

AIMWTS search in Aug 2015 revealed a total of 39 individuals with an aeromedical summary for one of the thrombocytopenic disorders. Breakdown of the cases showed 9 FC I/IA cases (3 disqualifications), 19 FC II cases (2 disqualifications), 9 FC III cases (2 disqualification), 2 ATC/GBC cases, and 0 MOD cases. All 7 disqualification cases were disqualified secondary to the thrombocytopenia diagnosis.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> for thrombocytopenia, ITP, or TTP should include the following:

- A. Comprehensive history and physical to include peripheral blood smear interpretation and course of platelets.
- B. CBC with differential.
- C. Bone marrow aspiration if over 60 years of age or associated symptoms suggest pathology.
- D. Hematology consultation.
- E. Cortisol stimulation test if treated with steroids for greater than 3 weeks (see systemic glucocorticoid waiver guide).
- F. Medical evaluation board (MEB) results for ITP, TTP and thrombocytopenia associated with splenomegaly.

The AMS for <u>renewal waiver</u> for thrombocytopenia, ITP, or TTP should include the following: A. Interim history and current exam.

- B. CBC quarterly (If individual has gone six years without recurrence then CBC just at waiver renewal time).
- C. Hematology consultation if platelets not stable since last waiver or platelets < 100 X 10<sup>9</sup>/L.

#### III. Overview.

Due to the diversity of underlying disorders, the differential diagnosis of thrombocytopenia is broad. These range from clinically insignificant pseudothrombocytopenia to life threatening disseminated intravascular coagulation and thrombotic thrombocytopenic purpura. As a result, a thorough history and physical exam as well as appropriate laboratory studies are essential in the search for an etiology.

Units can be a confusing factor when dealing with platelet results. It seems there is little standardization. All of the following results are equal:

| - |                       |                              |                       |  |
|---|-----------------------|------------------------------|-----------------------|--|
|   | $100 \times 10^9 / L$ | $100 \times 10^{3} / \Box L$ | $100,000/\text{mm}^3$ |  |

For the purposes of this waiver guide, the first of these units will be used.

Thrombocytopenia is defined as platelet count of <u>less than 150 X  $10^9/L$ </u>. Platelet counts of 100 X  $10^9/L$  to 150 X  $10^9/L$  are considered mild thrombocytopenia. However, the risk of bleeding with trauma or surgery is generally not increased until platelet counts are below 75 X  $10^9/L$ . Spontaneous

bleeding is unusual above  $30 \times 10^9/L$  so treatment is usually not initiated unless platelet counts fall below that level. Patients with platelet counts less than  $5 - 10 \times 10^9/L$  are considered at high risk for spontaneous, life-threatening hemorrhage.<sup>1</sup>

<u>Pseudothrombocytopenia (PTCP)</u>: The term pseudothrombocytopenia is used to define a state with a falsely low platelet count reported by automated hematology analyzers due to platelet clumping. Commonly, this clumping is caused by an alteration of the platelet surface glycoproteins when they are incubated with a calcium chelator such as EDTA. These modified platelet antigens then react to anti-platelet autoantibodies to form these large agglutinates. Some resources state that the aggregation of platelets in patients with EDTA-dependent PTCP can be prevented by the use of other anticoagulants such as sodium citrate or heparin, but even these agents can induce platelet clumping, and thus spuriously low platelet counts. Clumped platelets on peripheral blood smear are the hallmark. Repeat within 2 weeks with a peripheral smear. If platelet count is then normal, no further action is necessary.<sup>2</sup>

<u>Dilutional Thrombocytopenia</u>: This occurs with massive transfusion using platelet-poor fluids. The platelet count should be repeated when the patient is stable. The condition which required the transfusion will determine if waiver is required.

<u>Persistent Borderline Thrombocytopenia</u>: When platelet counts persist for 3 months in the range of  $100 \times 10^9$ /L and  $150 \times 10^9$ /L, other etiologies such as medications, viral infections or other transient conditions have been ruled out, and the aviator is asymptomatic and without other lab abnormalities, a waiver is not required. However, the 10-year probability of developing idiopathic thrombocytopenic purpura (platelet counts persistently <  $100 \times 10^9$ /L) was determined in one study to be 6.9%. In the same study, the 10-year probability of developing autoimmune disorders other than ITP was 12.0%. Therefore, complete blood count (CBC) is recommended every six months while on flying status.

Thrombocytopenia Secondary to Decreased Platelet Production: Many conditions can cause decreased platelet production; those likely to affect the previously healthy, flying population include viral infections, nutritional deficiencies, bone marrow disorders, drugs and toxins. A search for such underlying disorders is essential as some are life-threatening while others spontaneously resolve. Transient thrombocytopenia due to viral illness usually spontaneously resolves. Drugs known to occasionally induce thrombocytopenia include quinidine, quinine, sulfa preparations, carbamazepine, methyldopa, aspirin, oral antidiabetic drugs, gold salts, heparin, and rifampin. There are an estimated 87 known drugs with some evidence of causing thrombocytopenia.<sup>4</sup> Recent data indicates that up to 36% of patients on prolonged heparin therapy develop thrombocytopenia.<sup>5</sup> The mechanism is an immune reaction in which drug bound to the platelet membrane acts as a "foreign" antigen. The mechanism is analogous to the immune-mediated destruction of platelets that occurs in idiopathic thrombocytopenic purpura (ITP) and, except for the history of drug ingestion, the disorders are indistinguishable. When the drug is stopped, the platelet count typically begins to increase within 1 to 7 days; gold-induced thrombocytopenia is an exception, because injected gold salts may persist in the body for many weeks.

<u>Thrombocytopenia Secondary to Altered Distribution of Platelets</u>: Hypothermia is a cause of transient thrombocytopenia due to splenic sequestration. Because rewarming is associated with return to normal platelet count and function, the aeromedical concerns focus on the hypothermia

itself and are not discussed here. Congestive splenomegaly or hypersplenism is a more common and clinically significant cause of platelet sequestration and more than 200 diseases have been associated with congestive splenomegaly. The clinical and laboratory findings typically include significant splenic enlargement, platelet counts above 50 X 10<sup>9</sup>/L, and a decrease in red and/or white blood cell counts. Because the total pool of platelets is normal and mobilization typically occurs with stress, splenectomy is not clinically indicated in most cases. Splenomegaly is disqualifying for flying personnel; splenectomy is not without potential for complications and is not always curative, so great thought needs to be placed into this decision. Individuals should be immunized at least two weeks prior to splenectomy for *Streptococcus pneumoniae*, *Hemophilus influenzae* b, and *Neisseria meningitidis*.

<u>Thrombocytopenia Secondary to Increased Platelet Destruction</u>: These conditions, mainly idiopathic (immune) thrombocytopenic purpura, disseminated intravascular coagulation, and thrombotic thrombocytopenic purpura, manifest with purpura and/or bleeding.

*Idiopathic thrombocytopenic purpura (ITP)*: ITP is caused by autoreactive antibodies that bind to platelets and shorten their life span. ITP is an isolated thrombocytopenia, with otherwise normal blood counts, normal peripheral smear, and no clinically apparent associated conditions that may cause thrombocytopenia; it is a diagnosis of exclusion. ITP occurs more commonly in women during the second and third decades but can occur in either sex and at any age. Many patients come to medical attention with platelet counts between 5 and 20 X 10<sup>9</sup>/L because they develop petechiae, purpura, gingival bleeding or ecchymoses over the course of several days. Those with 30 to 50 X 10<sup>9</sup>/L often give history of easy bruising. The spleen size is normal. Platelet antibody testing is not necessary for management decisions in patients with ITP and the current available tests do not distinguish ITP from secondary thrombocytopenic purpura, and a negative test does not rule out the diagnosis of ITP.

In childhood, ITP is usually acute in onset and many cases resolve with and without treatment. If ITP was diagnosed in childhood (<18-years-old) and complete resolution was achieved, regardless of treatment, prognosis is excellent with no long term sequelae. Adult ITP (≥18-years-old) tends to be of more indolent onset with a course that is persistent, often lasting years, and can be characterized by recurrent exacerbations of disease. Of 86 patients that had a complete response, (despite treatment option) at 2 years, 9 had one or more relapses over the ensuing years of study (mean years of follow up was 10.5).

It is estimated that the lifetime risk of fatal hemorrhage for a person with ITP is approximately 5%. The risk of a nonfatal major hemorrhage was found to be 3% per year for patients less than 40 years of age. No conclusive data exist regarding the ability of clinical or laboratory parameters at presentation to predict the risk of major bleeding.

Treatment of ITP must be tailored to the individual patient with an attempt to match the risks of therapy with the severity of disease, taking into account the patient's lifestyle. Treatment is based primarily on the severity of the thrombocytopenia and bleeding. All suspect drugs should be discontinued. The goal of all treatment strategies for adult patients with ITP is to achieve a platelet count that is associated with adequate hemostasis, rather than a platelet count in the "normal" range. Treatment options include corticosteroids, splenectomy, and, for life-threatening bleeding, platelet transfusions and IV immune globulin. Adults usually are given an oral

corticosteroid (e.g. prednisone 1 mg/kg once/day) initially. In the patient who responds, the platelet count rises to normal within 2 to 6 weeks. The corticosteroid dosage is then tapered over one to four months. However, most patients (70 to 95%) either do not respond adequately or relapse as the corticosteroid is tapered; splenectomy can achieve a remission in about  $\frac{2}{3}$  of these patients. Of the 30 to 40% of adults that require therapy after splenectomy, the incidence of intracerebral hemorrhage ranges from 2 to 3% per year.

Thrombotic thrombocytopenic purpura (TTP): TTP and hemolytic-uremic syndrome (HUS) are acute, fulminant disorders characterized by thrombocytopenia, microangiopathic hemolytic anemia, fever, variable neurological symptoms, and renal failure. TTP and HUS involve nonimmunologic platelet destruction. Loose strands of fibrin are deposited in multiple small vessels, which damage passing platelets and RBCs. Platelets are also destroyed within multiple small thrombi. Multiple organs develop bland platelet-fibrin thrombi (without the vessel wall granulocytic infiltration characteristic of vasculitis) localized primarily to arteriocapillary junctions, described as thrombotic microangiopathy. TTP and HUS differ only in the relative degree of renal failure. Diagnosis and management in adults are the same. Therefore, in adults, TTP and HUS can be grouped together. Although most cases of TTP have no known etiology, potential causes and associations are pregnancy, deficiency of the plasma enzyme ADAMTS13, hemorrhagic colitis resulting from Shiga toxin-producing bacteria, and drugs (such as quinine, cyclosporine, mitomycin C).

Plasma exchange is the only treatment for TTP in adults which has firm data supporting its effectiveness. <sup>14</sup> In addition, glucocorticoid therapy is often prescribed. More intensive immunosuppressive therapy with rituximab, cyclophosphamide, vincristine or cyclosporine may be required in some individuals to obtain a remission. In one study relapses occurred in 20% of idiopathic TTP, most within the first year and in those with severe ADAMTS13 deficiency. Many patients describe persistent cognitive abnormalities for many years following recovery that can be documented by tests of new learning and recent memory.

### IV. Aeromedical Concerns.

Thrombocytopenia itself (apart from the underlying condition) is not likely to affect physical or cognitive performance unless bleeding occurs or the potential for trauma exists, which is inherent in many aeromedical occupations. ITP in adults is frequently a chronic disease that can require treatments not compatible with flying (steroids, immunosuppressive therapy). TTP is an acute, fulminant disease that has a high rate of relapse, especially in the first year. Furthermore, neurological system involvement is common, from seizures, cerebral vascular attacks to mild cognitive deficits. Resolution of symptoms and sequelae needs to be established.

| ICD-9 codes for thrombocytopenic disorders |                                  |  |
|--|----------------------------------|--|
| 287.3                                      | Primary thrombocytopenia         |  |
| 287.4                                      | Secondary thrombocytopenia       |  |
| 287.5                                      | Thrombocytopenia, unspecified    |  |
| 287.31                                     | Immune thrombocytopenic purpura  |  |
| 446.6                                      | Thrombotic microangiopathy (TTP) |  |

| ICD-10 codes for thrombocytopenic disorders |                                  |  |
|---|----------------------------------|--|
| D69.49                                      | Other primary thrombocytopenia   |  |
| D69.59                                      | Other secondary thrombocytopenia |  |
| D69.9                                       | Thrombocytopenia, unspecified    |  |
| D69.3                                       | Immune thrombocytopenic purpura  |  |
| M31.1                                       | Thrombotic microangiopathy       |  |

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#### WAIVER GUIDE

Updated: Jun 2016

Supersedes Waiver Guide of Jun 2012

By: Dr Christopher Keirns (ACS internist) and Dr Dan Van Syoc

Reviewed by Lt Col Roger Wood, AF/SG consultant for Hematology/Oncology

#### **CONDITION:**

Thrombocytosis (Jun 2016)

#### I. Waiver Consideration.

Platelet counts greater than  $400,000/\mu l$  are disqualifying for all flying classes, ATC/GBO, and SWA personnel, as well as for retention. If, after work-up, the elevation is determined to be reactive thrombocytosis secondary to an <u>acute</u> illness (e.g., surgery, infection) and the platelet count returns to normal, waiver is not required.

**Table 1: Waiver potential for thrombocytosis** 

| Flying Class     | Condition/Treatment            | Waiver Potential | ACS review/ |
|------------------|--------------------------------|------------------|-------------|
| (FC)             |                                | Waiver Authority | evaluation  |
| FC I/IA          | Sustained <u>reactive</u>      | Yes              | No          |
| Untrained II/III | thrombocytosis secondary to    | AETC             |             |
|                  | splenectomy.                   |                  |             |
|                  |                                |                  |             |
|                  | All other cases of sustained   | No               | No          |
|                  | thrombocytosis                 | AETC             |             |
| FC II/III        | Sustained <u>reactive</u>      | Yes              | No          |
| ATC/GBO          | thrombocytosis secondary to    | MAJCOM           |             |
| SWA              | splenectomy.                   |                  |             |
|                  |                                |                  |             |
|                  | Sustained <u>reactive</u>      | Maybe#*          | Yes         |
|                  | thrombocytosis not secondary   | AFMRA            |             |
|                  | to splenectomy.                |                  |             |
|                  | Essential thrombosytosis       | Marshat          | Yes         |
|                  | Essential thrombocytosis       | Maybe‡<br>AFMRA  | ies         |
|                  | without cytoreductive therapy. | AFWIKA           |             |
|                  | Essential thrombocytosis with  |                  |             |
|                  | cytoreductive therapy.         | No               | No          |
|                  | e j to reductive therapy.      | AFMRA            | 110         |
|                  | All other causes of primary    |                  |             |
|                  | thrombocytosis.                | No               | No          |
|                  |                                | AFMRA            |             |

<sup>#</sup> Depending on etiology; medical condition causing reactive thrombocytosis must be identified and also likely requires a waiver.

<sup>\*</sup> Waiver unlikely for untrained FC II and FC III personnel.

<sup>‡</sup> May be considered for waiver if ET does not require treatment, no history of thrombosis or hemorrhage, platelet count consistently below 1,000,000/µl, no evidence of JAK-2 and no other risk factors (e.g., tobacco use, hypertension, diabetes mellitus) and asymptomatic. Need for low-dose aspirin (eg, 81 mg/day PO) to control vasomotor symptoms may be considered acceptable following an ACS review. No waiver for untrained FC II and III.

AIMWTS search in Jun 2016 revealed a total of 16 cases submitted for a waiver with a diagnosis of thrombocytosis; 8 of the cases resulted in a disqualification. There were no FC I/IA cases, 3 FC II cases (2 disqualified), 9 FC III cases (3 disqualified), 1 ATC/GBC case (disqualified) and 3 MOD cases (2 disqualified).

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial</u> waiver for thrombocytosis should include the following:

- A. Comprehensive history to include thrombosis or bleeding episodes (negatives included), symptoms, course of platelet values, treatment, and cardiac risk factors.
- B. Physical complete, special attention to skin, neurology and abdomen.
- C. Current CBC with differential and peripheral smear.
- D. Serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein, Janus kinase 2 (JAK2) gene mutation testing, and all other ancillary testing deemed appropriate by the treating specialist.
- E. Hematology consultation to include bone marrow biopsy and clonal markers.
- F. MEB results if required.

The AMS for <u>renewal</u> waiver for thrombocytosis should include the following:

- A. History summary of initial history (platelets, bone marrow, clonal markers) and symptoms (negatives included).
- B. Physical skin, neurology, abdomen.
- C. CBC at least annually (minimum every 6 months for ET) or more frequently at direction of hematologist.
- D. Updated hematology consultation.

#### III. Overview.

Thrombocytosis, also called thrombocythemia, is generally defined as a platelet count greater than a defined upper limit of normal that usually falls between 350,000/µl to 450,000/µl, depending on the laboratory or medical reference. In one study of 10,000 adult subjects from Italy, the 99<sup>th</sup> percentile for the platelet count was 409,000/µl for men and 381,000/µl for women.¹ The most commonly cited cut off for normal is often arbitrarily defined as <450,000/µl as this has also been chosen as one of the criteria required for the diagnosis of essential thrombocythemia by the World Health Organization. It is estimated that a platelet count in excess of 450,000/µl occurs in about 2.5% of the population (regardless of sex and ethnicity).² Elevated platelet counts are often an incidental or unexpected finding on a complete blood count (CBC) conducted to evaluate an unrelated condition.³ For those individuals found to have thrombocytosis without associated bleeding or thrombosis, the first challenge is to find the underlying cause.

The causes of thrombocytosis are separated into two categories: autonomous (primary) thrombocytosis and reactive (secondary) thrombocytosis. Autonomous (or clonal) thrombocytosis occurs as a result of myeloproliferative disorders, myelodysplastic disorders, or more rarely as a result of a hereditary condition.<sup>4</sup> Reactive thrombocytosis is most often a normal physiologic

response to a coexistent inflammatory condition (e.g., infection, chronic inflammatory condition). Distinction between these two categories is important since autonomous thrombocytosis is associated with a significantly increased risk for thrombotic or hemorrhagic complications whereas reactive thrombocytosis is not.<sup>5</sup> The association of autonomous thrombocytosis with vasomotor symptoms (headache, visual symptoms, lightheadedness, atypical chest pain, acral dysesthesia, erythromelalgia), thrombosis and hemorrhagic complications is well established.<sup>6,7,8</sup> As administration of low-dose aspirin (eg, 81 mg/day PO) is often effective for controlling vasomotor symptoms resulting from microvascular inflammation, platelet aggregation and arteriolar microthrombi formation, the most aeromedically relevant complications of thrombocytosis are felt to be the future risk of hemorrhage and thrombotic events.

# A. Reactive (secondary) thrombocytosis

The most common reason for an elevated platelet count is reactive thrombocytosis.<sup>5</sup> Studies have concluded that as many as 70 to 90% of all patients with clinically elevated platelet counts have reactive thrombocytosis.<sup>9, 10, 11, 12</sup> Reactive thrombocytosis is most often a normal physiologic response to a coexistent inflammatory condition or surgery. Lifetime reactive thrombocytosis may also be present in patients who have had a splenectomy.

Reactive thrombocytosis is generally a self-limiting condition that resolves with the inciting condition. As mentioned above, reactive thrombocytosis is felt to have little excess associated thrombotic or hemorrhage risk above that of the underlying causative etiology. However, in cases of extreme reactive thrombocytosis (platelet counts >1,000,000/μL) rates of patients experiencing a significant thrombosis and hemorrhage have been shown to be 1% and 3%, respectively.<sup>6, 12</sup> The list of conditions that may lead to a reactive thrombocytosis is lengthy. The platelet count should normalize within days after "correction" of whatever problem caused the thrombocytosis. A more prolonged elevation of the platelet count suggests an undiagnosed problem, such as a persistent infection. Common conditions include tissue damage from surgery, infection, malignancy, trauma, asplenia, and chronic inflammatory disorders.<sup>8</sup> Other conditions associated with transient thrombocytosis include acute blood loss, "rebound" from thrombocytopenia, iron deficiency, and even exercise.<sup>3, 8</sup>

Reactive thrombocytosis may be a result of a subclinical disorder or occult cancer. Therefore, asymptomatic patients with thrombocytosis must have a comprehensive physical evaluation for malignancy or other potentially treatable disease. The elevated platelet count needs to be confirmed by repeat testing on a different day.

#### B. Autonomous (primary) thrombocytosis

- 1) Myeloproliferative disorders:
- a) <u>Polycythemia vera</u> (PV) causes thrombocytosis with an increase in blood viscosity. Thrombosis in the brain or other vital organs is a significant threat for PV patients.<sup>13</sup> Thrombocytosis secondary to PV is not felt to be an aeromedically waiverable condition.
- b) <u>Chronic myeloid leukemia</u> (CML) The leukemias have many significant medical complicating factors other than thrombocytosis that have the potential for progression and performance

decrement in the aviation environment. Aeromedical waivers for successfully treated CML are evaluated on a case-by-case basis. (See leukemia waiver guide.)

- c) <u>Primary myelofibrosis</u> (PMF) PMF is characterized by the presence of bone marrow fibrosis that cannot be attributed to another myeloid disorder. PMF will often present with anemia, marked splenomegaly, early satiety, and hypercatabolic symptoms including severe fatigue, low-grade fever, night sweats and weight loss. Prognosis for this condition is often poor with a median survival of just 5 years. Thrombocytosis associated with PMF is not felt to be an aeromedically waiverable condition.
- d) <u>Essential thrombocytosis</u> (ET) is a diagnosis of exclusion as it is not a cytogenetically or morphologically defined disease entity. It tends to be a disorder of adults in the sixth or seventh decade of life. The median age at diagnosis for ET is 60 with as many as 20 percent being younger than 40. There appears to be a slight female preponderance in ET cases with an estimated prevalence of 24 total cases/100,000 population. No single specific clinical, cytogenic, or molecular test is available for the diagnosis. Janus kinase 2 (JAK2) gene mutation present in 95% of polycythemia vera cases, is also present in 50% of ET cases. ET should be suspected in the asymptomatic patient found to have a chronically unexplained elevated platelet counts, an intact spleen, and normal serum ferritin and C-reactive protein level. The criteria for making this diagnosis has been proposed by the World Health Organization and must include all four of the below items.
- i. A platelet count greater than or equal to  $450,000/\mu L$ .
- ii. A bone marrow biopsy consistent with ET.
- iii. A lack of any criteria for PV, CML, myelofibrosis, or myelodysplastic syndromes.
- iv. The demonstration of a JAK2 mutation or other clonal marker; or in the absence of a clonal marker, no evidence for reactive thrombocytosis.

Most commonly, ET is found incidentally on complete blood counts (CBCs), but less commonly it may be found due to complications. Complications of ET can generally be categorized into thrombotic, hemorrhagic, or progression into one of the other three myeloproliferative disorders.<sup>3</sup> Determinants of an increased risk for complications are generally agreed upon to be age over 60, previous thrombotic event, presence of cardiovascular risk factors (e.g., tobacco use, hypertension, diabetes mellitus), presence of JAK2 mutation, and platelet counts >1,000,000/μL. The annual risk of thrombotic complications in an older case-control study of patients with ET reported in 1990, found the overall risk of thrombotic episodes to be 6.6%/patient-year compared with 1.2%/patientyear in the control group. 18 In this cohort, the most common thrombotic event was a cerebral arterial thrombosis and the corresponding risks for hemorrhagic complications were documented to be much lower (0.33 vs 0 percent/patient year, respectively). The most significant risk factors for thrombosis identified in this historical study were a history of prior thrombosis (31.4%/patient-year) and age over 60 (15.1%/patient-year). Newer studies continue to support the adverse prognostic value of a history of prior thrombosis as well as older age in ET, however these more recent estimates of thrombotic risk have been found to be lower than that reported in the 1990 study. 19,20 The risk of hemorrhage or progression to another myeloproliferative disorder is also less than that of a thrombotic event.<sup>20</sup>

Treatment of ET is generally categorized into one of two types of therapy. Aspirin therapy is indicated for relief of vasomotor symptoms and to reduce the risk of microvascular complications.

It is very important to emphasize that aspirin therapy in these patients is not without risk. ET patients with platelet counts over 1,500,000/µl may develop an acquired von Willebrand's disease. Aspirin in these select patients likely increases their risk of hemorrhagic complications. The second category of therapy for ET is cytoreductive therapy. Cytoreductive therapy is generally felt to be of benefit to ET patients at high-risk of complications (age > 60 or a previous history of thrombosis). The two more common cytoreductive agents used are the antimetabolite hydroxyurea and the oral imidazoquinazoline derivative anagrelide.<sup>21</sup> These drugs are <u>not</u> approved for flying status. Furthermore, even if one were to reduce the platelet count to normal range with a cytoreductive drug complication rates still exceed acceptable aeromedical standards (probably because the platelets are still qualitatively abnormal and the fact that only ET patients predicted to be at high risk for complications would be treated with cytoreductive therapy). For patients at high risk for vascular events, some researchers feel that the combination of hydroxyurea and low-dose aspirin is superior to anagrelide plus low-dose aspirin.<sup>22</sup>

- 2) Myelodysplastic disorders cause different degrees of cytopenia and abnormal cell maturation. These patients are therefore at increased risk of anemia, infection, and bleeding which are often refractory to treatment. Thrombocytosis in less commonly seen in myelodysplastic disorders than thrombocytopenia, but it has been described in 5q- syndrome, and refractory anemia with ring sideroblasts and thrombocytosis (RARS-T).<sup>6</sup> Thrombocytosis associated with myelodysplastic disorders is not felt to have aeromedical waiver potential.
- 3) Hereditary or congenital thrombocytosis is a rare and heterogeneous genetic disorder that can present clinically like ET (e.g., vasomotor symptoms). This autosomal dominant condition usually presents at birth but can be discovered at any time during life. Diagnosis should be considered following discovery of thrombocytosis in a young patient with otherwise unexplained thrombocytosis as well as a positive family history. Genetic testing would be required to confirm germline mutations in the *THPO* gene or in the *MPL* gene. Hereditary thrombocytosis may increase risk for thrombosis and hemorrhagic events, but it is not felt to cause myeloproliferation.

#### **Evaluation**

The current USAF policy is that any platelet count >400,000/µl must be evaluated prior to continuation of aviation and other military duties. The basic approach to an individual found to have an elevated platelet count should begin with an evaluation for reactive thrombocytosis. As stated above, reactive thrombocytosis is the most common reason for an elevated platelet count and is usually associated with infections, inflammation, trauma, hemolysis, metastatic cancer, asplenia, or iron deficiency anemia. If the platelet count returns to normal after management of the inciting condition, the individual may be returned to duty or flying status as long as the precipitating cause itself is not disqualifying. The presence of chronic thrombocytosis, vasomotor symptoms, thrombohemorrhagic complications, or splenomegaly would all be potential indicators of autonomous (primary) thrombocytosis. Further diagnostic testing would be necessary to distinguish among the different causes of autonomous (primary) thrombocytosis.

In general, persistent thrombocytosis in an aviator should prompt a formal hematology consultation who will guide the diagnostic workup. The laboratory evaluation of thrombocytosis will usually begin with review of the complete blood count (CBC) and peripheral smear. Clues on the peripheral smear indicating a reactive thrombocytosis would be the presence of microcytic anemia

(iron deficiency) or Howell-Jolly bodies (asplenia or functional hyposplenism). Alternatively, an underlying myeloproliferative disorder could be suggested by an increase in hematocrit or leukocyte counts on the CBC. Initial laboratory testing will also normally include measurement of a serum ferritin, ESR and C-reactive protein. These labs would be expected to be increased with a reactive thrombocytosis. Of note, a normal serum ferritin level is also useful in excluding the possibility of iron deficiency anemia as the cause of a reactive thrombocytosis. According to the World Health Organization, JAK2 mutation screening is also part of the diagnostic workup for thrombocytosis. Finally, patients in which a reactive etiology to the thrombocytosis cannot be identified will require a bone marrow examination, which would include testing for the Ph+ chromosome. Patients with a reactive thrombocytosis will have normal appearing bone marrow morphology as well as negative JAK2 mutation screening.

#### IV. Aeromedical Concerns.

The aeromedical concerns associated with an aviator with thrombocytosis will depend largely upon the underlying causative etiology.

A. <u>Autonomous (primary) thrombocytosis</u>. As outlined above, not all causes of primary thrombocytosis are felt to have aeromedical waiver potential. Primary thrombocytosis is often associated with an increased risk for thrombotic or hemorrhagic complications that exceeds acceptable aeromedical risk thresholds. In an aviator determined to have an active primary thrombocytosis, only the subset of low-risk essential thrombocytosis that is not requiring of cytoreductive therapy is felt to have waiver potential.

B. Reactive (secondary) thrombocytosis. Thrombotic and hemorrhagic complications are not a significant aeromedical concern in reactive thrombocytosis unless the underlying condition itself predisposes to such complications (e.g., individuals who are post-operative or with malignancy).<sup>5</sup> The elevated platelet count by itself is not expected to cause complications that affect physical or cognitive performance. For the condition to be labeled a reactive thrombocytosis, a credible underlying etiology must be identified. Individuals who have had a surgical splenectomy frequently have lifelong reactive thrombocytosis and once again do not have an increased risk for thrombosis or bleeding.<sup>4,11</sup> (See splenectomy waiver guide.)

| ICD-9 Codes for Thrombocytosis |   |  |
|--------------------------------|---|--|
| 238.71                         | Essential thrombocythemia (primary                |  |
|                                | thrombocytosis)                                   |  |
| 238.4                          | Polycythemia                                      |  |
| 205.1                          | Chronic myelomonocytic leukemia                   |  |
| 238.75                         | Myelodysplastic syndrome, unspecified             |  |
| 238.76                         | Myelofibrosis with myeloid metaplasia (idiopathic |  |
|                                | myelofibrosis [chronic])                          |  |

| ICD-10 Codes for Thrombocytosis |   |  |
|---------------------------------|---|--|
| D47.3                           | Essential (hemorrhagic) thrombocythemia |  |
| D45                             | Polycythemia vera                       |  |
| C92.1                           | Chronic myeloid leukemia                |  |
| D46.9                           | Myelodysplastic syndrome, unspecified   |  |
| D47.1                           | Chronic myeloproliferative disease      |  |

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#### WAIVER GUIDE

Updated: Mar 2015

Supersedes: Waiver Guide of Mar 2012

By: Maj Benjamin J. Park (RAM 16) and Dr. Dan Van Syoc

Reviewed by Lt Col Mark True, AF/SG consultant for Endocrinology

#### **CONDITION:**

**Thyroid Cancer (Mar 2015)** 

#### I. Waiver Considerations.

History of thyroid cancer is disqualifying for all flying classes. All malignancies require an MEB, and all malignant neoplasms that are unresponsive to therapy or have residuals of treatment or not fitting for further service. Waivers will be considered for Flying Class II and III individuals and RPA Pilots with minimal or no residual disease on monitoring who do not have post-operative hypoparathyroidism, hypocalcemia, or recurrent laryngeal nerve damage, unless those conditions have been adequately treated.

Table 1: Waiver potential of thyroid cancer

| Flying Class (FC) | Condition  | Waiver Potential<br>Waiver Authority | ACS review/evaluation |
|-------------------|------------|--------------------------------------|-----------------------|
| I/IA              | All stages | Yes#†                                | Yes                   |
|                   |            | AETC                                 |                       |
| II/III            | All stages | Yes#+†                               | Yes                   |
| ATC/GBO/SWA       |            | MAJCOM                               |                       |

<sup>#</sup> For FC I/IA and other untrained personnel waiver may be considered after 2 years of remission, asymptomatic.

Review of AIMWTS through November 2014 showed 87 cases of thyroid cancer. Breakdown of the cases revealed: 1 FC I/IA, 46 FC II, 22 FC III, 5 ATC/GBC, and 13 MOD; 7 were disqualified. Of the seven disqualifications (3 FC II, 2 FC III, 1 MOD, & 1 ATC), 4 were disqualified due to a concomitant disqualifying diagnosis, 1 due to failure to provide additional requested info, 1 due to inadequate time lapse since treatment, and one because, as a nurse, the member could not deploy due to an assignment limitation code.

### II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for <u>initial waiver</u> for thyroid cancer should include the following:

A. History – symptoms, pathology, stage, treatment, including date of last treatment and radioactive iodine scans and treatments, surveillance plan, levothyroxine dose, and activity level.

B. Physical – Neck exam.

<sup>+</sup> For trained personnel, waiver may be considered six months after treatment completed, in remission and asymptomatic.

<sup>†</sup> No indefinite waivers.

- C. Endocrinology and surgeon reports to include six-month follow-up.
- D. Labs All thyroid function tests to include: TSH, serum thyroxine, Tg, and Tg antibodies. (CEA and calcitonin are relevant if medullary cancer, as are screening tests for appropriate MEN syndromes)
- E. Reports of any imaging studies, if done.
- F. Tumor board report, military or civilian, if applicable.
- G. Medical evaluation board results.

The AMS for <u>waiver renewal</u> of thyroid cancer should include the following:

- A. History brief summary of stage, treatment, frequency of surveillance and results, any symptoms, activity level.
- B. Physical Neck exam.
- C. Endocrinology consult.
- D. Labs all thyroid function test results since previous waiver. (include Tg and Tg antibodies, and CEA, calcitonin if medullary cancer)
- E. Reports of any imaging studies, if done.

#### III. Overview.

Thyroid cancer is the most common endocrine tumor representing 3.8% of all new cancer cases in the US.<sup>1</sup> There are four histologic types of thyroid cancer: papillary, follicular, medullary, and anaplastic.<sup>2</sup> The papillary and follicular histotypes are termed differentiated thyroid carcinoma and represent more than 90% of all thyroid cancers.<sup>3</sup> Medullary is a neuroendocrine tumor representing 5%, and anaplastic carcinomas, termed poorly differentiated carcinoma, are responsible for 1.7% of all thyroid cancers.<sup>4, 5</sup> More rare are the thyroid lymphomas or other carcinomas which metastasize to the thyroid.

Over the last two decades, the incidence of thyroid cancer has risen globally to the point where it is now the most common endocrine malignancy.<sup>6</sup> In the U.S., the risk is now more than twice what it was in 1990.<sup>7</sup> The current overall estimated incidence is 12.9 per 100,000, with rates of new thyroid cancer rising on average of 5.5% each year over the past 10 years.<sup>1</sup> Papillary carcinoma demonstrates the greatest proportional increase over time.<sup>8, 9, 10</sup> Rates for follicular, medullary, and anaplastic types, particularly among women, continue to rise across most age ranges. This is especially true for anaplastic carcinomas.<sup>8</sup>

Much of the perceived increase may well be due to improved detection of small papillary cancers, and many thyroid experts feel that this "increase" is actually due to improvements in diagnostic techniques such as ultrasound, imaging studies and ultrasound-guided fine needle biopsy (FNAB).<sup>11</sup> For 2014, the American Cancer Society reports approximately 62,980 new cases of thyroid cancer in the U.S. alone, of which 47,790 (76%) were in women, and 15,190 in men. Of these, nearly 2/3 were diagnosed in patients younger than 55 years of age with 2% occurring in children and teens.<sup>7</sup>

There may also be a role for genetic testing in the future of thyroid cancer diagnosis and treatment, particularly for "inconclusive" cytologic results. A 2011 study of 82 FNA smears, 46 malignant and 36 benign by histology looked to quantify the expression levels of the c-KIT gene by quantitative Real Time PCR. The researchers found a highly preferential decrease in c-KIT

transcription for malignant thyroid lesions compared to the benign ones. Their analysis proved to be highly specific and sensitive, improving the cytological diagnostic accuracy by 15%. 12

In general, 5% of thyroid nodules represent thyroid cancer.<sup>13</sup> Fortunately, the prognosis is usually excellent, with most forms of the disease (apart from the fulminant and lethal anaplastic variety) running an indolent course. Overall the relative 10-year survival rate is better than 90% (second only to non-melanoma skin cancer), and has remained fairly stable. From 2007-2011, the number of deaths from thyroid cancer was 0.5 per 100,000 men and women per year, with death rates rising on average of 0.8% per year.<sup>1</sup> In 2011 the American Cancer Society reported 1,740 deaths from thyroid cancer, of which 980 (56%) were women and 760 men.<sup>7</sup>

Most thyroid cancers are diagnosed at a local stage (61%), occur in non-Hispanic whites (79.5%), and in females. A 2011 study published by the National Cancer Institute found that among women, papillary thyroid cancer rates were highest among Asians (10.96 per 100,000 woman-years) and lowest among blacks (4.90 per 100,000 woman-years), while follicular cancer rates did not vary substantially by race or ethnicity. Medullary cancer rates were highest among Hispanics (0.21 per 100,000 woman-years) and whites (0.22 per 100,000 woman-years), and anaplastic rates were highest among Hispanics (0.17 per 100,000 woman-years). Among men, both papillary and follicular thyroid cancer rates were highest among whites (3.58 and 0.58 per 100,000 man-years, respectively), medullary cancer rates were highest among Hispanics (0.18 per 100,000 man-years), and anaplastic rates were highest among Asians (0.11 per 100,000 man-years).

### **Papillary Thyroid Cancer**:

- Age at diagnosis: Most frequently 30-50 years old, with a peak at age 50, and a female-to-male ratio of about 2.5:1.14
- Clinical Course: Indolent and slow-growing both in the thyroid gland and in secondary sites. Tends to metastasize locally to lymph nodes and strap muscles of the neck. The presence of local cervical adenopathy does not adversely affect prognosis. It can rarely metastasize to the lungs, bone or brain. Lesions less than 1 cm at diagnosis (micropapillary) have a lifetime recurrence rate of about 5% and no change in death rate from the general population. There is an increased incidence in high iodine intake regions, as well as in those receiving external radiation to the neck as a child.<sup>15</sup>
- Pathologic Variants: Can see Follicular, Tall Cell, or Columnar Cell variants which confer a worse prognosis.
- Prognosis: Excellent. Ten year overall survival is 93%. Patients younger than 40 years have better prognosis than older patients.

Table 2: Papillary thyroid cancer\*

| Stage | 5-Year Relative Survival |  |
|-------|--------------------------|--|
|       | Rate                     |  |
| I     | Near 100%                |  |
| II    | Near 100%                |  |
| III   | 93%                      |  |
| IV    | 51%                      |  |

<sup>\*</sup>Based on patients diagnosed 1998 to 1999<sup>17</sup>

#### Follicular Thyroid Cancer:

- Age at diagnosis: Older population than papillary tumors; peak incidence between ages 40 and  $60.^{18}$
- Clinical Course: Tends to metastasize hematogenously to bone and lungs. Often a bone lesion (lytic lesions and pathologic fractures) is the presenting symptom. Small primary lesions in the thyroid may be overlooked. More commonly seen in iodine-deficient regions.
- Prognosis: Excellent; survival slightly less than with papillary cancer; estimated to be about 85% at ten years. 19 Older patients have a worse prognosis.

Table 3: Follicular thyroid cancer\*

| Stage | 5-Year Relative Survival |  |
|-------|--------------------------|--|
|       | Rate                     |  |
| I     | Near 100%                |  |
| II    | Near 100%                |  |
| III   | 71%                      |  |
| IV    | 50%                      |  |

<sup>\*</sup>Based on patients diagnosed 1998 to 1999<sup>17</sup>

### Anaplastic or Undifferentiated Thyroid Cancer:

- Age at diagnosis: mean age at diagnosis is 65 years and fewer than 10 percent are younger than 50 years. <sup>20</sup>
- Clinical Course: Typical presentation is an older patient with dysphagia, cervical tenderness, and a painful, rapidly enlarging neck mass. Superior vena cava syndrome may also be present, as well as metastatic disease which is found in 30-50% of new diagnoses.<sup>21</sup> Other symptoms may include stridor, and/or hoarseness. Extremely rapid growth and local invasion can lead to strangulation or esophageal obstruction. While exact figures vary, there may be a history of differentiated thyroid cancer which has undergone transformation.
- Prognosis: Grave in spite of combined surgery, radiation, and chemotherapy. Median survival is 5 months; with a one year survival of 20%.<sup>22</sup> All anaplastic carcinomas are considered Stage IV, and have a 5-year relative survival rate around 7% (based on patients diagnosed between 1985 and 1991).<sup>19</sup> Poor prognosis is associated with acute symptoms (within 1 month of presentation with neck tumor, rapid growth, hoarseness, pain, dyspnea, or dysphagia), tumor >5 cm, distant metastases, or a white blood cell count of >10,000.

### Medullary Thyroid Cancer:

General: Neuroendocrine tumors arising from parafollicular C cells which produce thyrocalcitonin. Sporadic disease is typically seen in older individuals (50-60) and accounts for 80% of cases. Of these 75-95% present as a solitary thyroid nodule; typically in the upper thyroid lobes. The other 20% have inherited tumor syndromes. These syndromes are all autosomal dominant and can be detected with genetic testing. The syndromes are multiple endocrine neoplasia (MEN) type 2A (medullary carcinoma of the thyroid, pheochromocytoma, and multigland parathyroid hyperplasia or tumors), MEN 2B (medullary carcinoma of the thyroid, pheochromocytoma, mucosal neuromas, and marfanoid body habitus), or familial medullary carcinoma. All three involve mutations in the *RET* proto-oncogene and should be suspected in

younger patients who present with medullary histology.<sup>24</sup> Lymph nodes are involved pathologically in two-thirds of all cases.<sup>25</sup>

- Clinical Course: Two patterns a unifocal lesion occurring sporadically in elderly and a bilateral form often associated with pheochromocytomas which tend to be malignant (autosomal dominant MEN type 2). Clinical syndromes include asymptomatic elevated serum calcitonin, intractable diarrhea, Cushing's syndrome, and carcinoid syndrome.
- Prognosis: Overall 10/15 year survival rates approximately 70/65% in the previous studies. When the familial forms were excluded these rates dropped to about 60 and 54% respectively. Younger age at diagnosis, smaller tumor size, and familial form are all associated with better survival rates. Two groups of patients have 10-15 year survival rates no different from the general population: 1) Patients with the familial form identified by screening (serum calcitonin determinations in relatives of patients with medullary thyroid cancer), and 2) Young patients with tumors <1 cm in size and clinical stage I or II at diagnosis. If local lymph node metastases are identified or when the preoperative serum basal calcitonin is >400 pg/mL, the 2009 American Thyroid Association (ATA) Guidelines suggest additional cross sectional imaging including chest CT, neck CT, three-phase contrast-enhanced liver CT or contrast-enhanced liver MRI are indicated.<sup>26</sup> Given that any medullary carcinoma may be associated with MEN 2, preoperative testing must also include measurement of serum calcium (to rule out hyperparathyroidism requiring concomitant surgical intervention), plasma fractionated metanephrines as the initial screen for pheochromocytoma, as well as serum calcitonin concentration to establish if the tumor is capable of hypersecreting the hormone. In the case of elevated calcitonin, post-operative values should also be followed as postoperative doubling time has been shown to be a prognostic factor for survival rates.<sup>27</sup>

Table 4: Medullary thyroid cancer\*

| Stage | 5-Year Relative Survival<br>Rate |
|-------|----------------------------------|
| I     | Near 100%                        |
| II    | 98%                              |
| III   | 81%                              |
| IV    | 28%                              |

<sup>\*</sup>Based on patients diagnosed between 1985 and 1991<sup>17</sup>

<u>Pathogenesis</u>: Exposure to either external (usually for benign conditions) or ingested radiation in childhood significantly increases the incidence of thyroid cancer. Such exposures result in a higher rate of PTC oncogene mutation than that found in thyroid tumors which do not result from such exposure. By contrast, BRAF gene mutation is less common in such thyroid tumors. Predisposing factors are the dose of radiation (direct correlation), female sex, and younger age at time of irradiation. The carcinogenic effect of irradiation on the thyroid persists for at least 40 years. All patients should be asked about any history of head or neck irradiation in infancy or childhood.

# Staging of Thyroid Cancer

Table 5: American Joint Committee on Cancer (AJCC) Thyroid Cancer Staging System.<sup>19</sup>

| Stage (T) | Primary Tumor (T)  |
|-----------|--|
| T1        | Tumor 2 cm or lesion greatest dimension limited to the thyroid   |
| T2        | Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid   |
| T3        | Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroidal extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues) |
| T4a       | Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve                                       |
| T4b       | Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels   |
|           | All anaplastic carcinomas are considered T4 tumors   |
| T4a       | Intrathyroidal anaplastic carcinoma – surgically resectable  |
| T4b       | Extrathyroidal anaplastic carcinoma – surgically unresectable  |
|           | Regional Lymph Nodes   |
| NX        | Regional lymph nodes not assessed  |
| N0        | No regional lymph node metastasis  |
| N1        | Regional lymph node metastasis   |
| N1a       | Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)  |
| N1b       | Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes   |
|           | Distant Metastasis   |
| MX        | Distant metastasis cannot be assessed  |
| M0        | No distant metastasis  |
| M1        | Distant metastasis   |

Table 6: AJCC Stage Grouping for Thyroid Cancer. 19

Papillary or Follicular, Under 45 Years of Age

| Stage | <b>Primary Tumor</b> | Regional Lymph Nodes | Distant Metastasis (M) |
|-------|----------------------|----------------------|------------------------|
|       | (T)                  | (N)                  |                        |
| I     | Any T                | Any N                | M0                     |
| II    | Any T                | Any N                | M1                     |

Papillary or Follicular, 45 Years of Age and Older and all Medullary Carcinomas

| Stage | <b>Primary Tumor</b> | Regional Lymph Nodes | Distant Metastasis (M) |
|-------|----------------------|----------------------|------------------------|
|       | <b>(T)</b>           | (N)                  |                        |
| Ι     | T1                   | N0                   | M0                     |
| II    | T2                   | N0                   | M0                     |
| III   | T3                   | N0                   | M0                     |
|       | T1                   | N1a                  | M0                     |
|       | T2                   | N1a                  | M0                     |
|       | T3                   | N1a                  | M0                     |
| IVA   | T4a                  | N0                   | M0                     |
|       | T4a                  | N1a                  | M0                     |
|       | T1                   | N1b                  | M0                     |
|       | T2                   | N1b                  | M0                     |
|       | T3                   | N1b                  | M0                     |
|       | T4a                  | N1b                  | M0                     |
| IVB   | T4b                  | Any N                | M0                     |
| IVC   | Any T                | Any N                | M1                     |

<u>Diagnosis</u>: Carcinoma is a concern in any thyroid nodule. Therefore, all thyroid nodules should be evaluated by an Endocrinologist, ENT surgeon, or someone with experience in the evaluation. The initial evaluation of a thyroid nodule includes a thorough history to include family history for thyroid disease and a personal history of radiation exposure. A TSH should always be checked.<sup>2</sup> A thyroid scan (I<sup>123</sup>) is indicated if the TSH is suppressed since hyper-functioning or "hot" nodules are essentially never malignant. Hot nodules require no further workup or treatment except ablation if the patient is hyperthyroid. All nodules >1.5 cm, and those <1.5cm with risk factors, should be sampled using fine-needle aspiration for cytology. If an adequate sample is obtained, cytology can accurately diagnose papillary, medullary, and anaplastic carcinoma cells. Approximately 15-25% of aspirations are "inconclusive" or "inadequate". About 20-40% of the suspicious (inconclusive) lesions may be carcinoma. For nodules with benign cytologic results, recent series report a higher false negative rate with palpation FNA (1-3%) than with ultrasound FNA (0.6%).<sup>28</sup> Therefore, thyroid nodules that are not removed need continued follow-up with repeat evaluation if there is evidence of significant size increases. A significant increase in size is defined as an increase of 20% in at least one dimension and an increase of at least 0.2 cm in two dimensions.

<u>Treatment</u>: Managing differentiated thyroid cancers can be a challenge as there have been limited prospective randomized trials of treatment. In general, thyroid malignancies are treated surgically, though there is some research underway on the use of High-intensity Focused Ultrasound Ablation (HIFU) therapy.<sup>16</sup> The extent of surgery is normally determined by cancer type, but most thyroid experts now advise total or near-total thyroidectomy for all patients with a preoperative diagnosis,

as this leads to an improved disease-free survival. The major concern with thyroidectomy is hypoparathyroidism and recurrent laryngeal nerve injury. Many cases of hypoparathyroidism are transient.

Most papillary and follicular carcinomas are also treated with radioactive iodine ( $I^{131}$ ) and suppressive doses of thyroxine. The goal of radiotherapy is to destroy any residual microscopic thyroid tissue.<sup>29</sup> In most institutions, a post-therapy scan is done a week after treatment with  $I^{131}$ . This post therapy scan is highly sensitive for residual disease not seen on diagnostic scans.

About 5-15% of patients become refractory to radioactive iodine and prognosis is poor in these individuals with a 5 year survival rate of 66%. Few treatment options exist while standard chemotherapy has shown little benefit.<sup>30</sup> There is some potential with targeted systemic agents that target vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF) and may act by depriving tumor vascular supply.<sup>30</sup> The most extensively evaluated of these targeted therapies include sorafenib (approved for use in Nov 2013) and lenvatinib (currently in phase II and III) which are multikinase inhibitors that inhibit VEGF and PDGF receptors. In the DECISION trial, progression free survival was 10.8 months vs. 5.8 months in patients treated with sorafenib vs. placebo.

Treatment with thyroxine, besides replacing thyroid function in patients who have undergone near-total thyroidectomy, is to minimize release of TSH. The dose of thyroxine is based on the patient characteristics. Lower risk patients are given doses to keep TSH in the low-normal range. Higher risk patients and those with some evidence of residual disease are usually treated with a goal of keeping the TSH undetectable with the minimum of symptoms. Patients need life-long regular follow-up to identify local recurrence or lung metastases. Unlike differentiated thyroid cancer, anaplastic carcinoma responds poorly to treatment. Palliative or debulking therapies are done in conjunction with radiation and chemotherapy with limited success. Treatment of medullary thyroid carcinoma is also surgical, but more aggressive cervical dissections are indicated. Post-surgery, patients are monitored by following the levels of calcitonin as a tumor marker. Persistent elevations of calcitonin indicate residual disease. Those with near normal post-operative calcitonin values can be followed clinically, but those with levels >100 pg/ml of calcitonin should be evaluated for other resectable lesions.

Monitoring: Follow-up is done using thyrotropin stimulated I<sup>123</sup> or I<sup>131</sup> scanning and/or thyroglobulin (Tg) measurements with or without recombinant thyrotropin (rhTSH) stimulation. A positive scan or persistent elevations of thyroglobulin can indicate residual carcinoma or recurrence. (This is only true if the patient had a total thyroidectomy with ablation of any remaining thyroid tissue; otherwise, residual normal thyroid tissue can give false positive results.) Thyrotropin stimulation is done by thyroid hormone withdrawal for 6-8 weeks to induce hypothyroidism or by rhTSH injections on two consecutive days. The former has the advantage of being more sensitive, but is much less convenient for the patient and requires the patient to be hypothyroid and DNIF. Recombinant thyrotropin stimulation is much better tolerated by the patients since the hypothyroid symptoms are avoided and can now be used for treatment as well as follow-up. Most recurrences are localized to the thyroid bed or cervical lymph nodes and occur within 5 years of diagnosis. Recurrences are also treated with surgery and/or radioactive iodine.

Due to the relatively indolent nature of differentiated thyroid carcinoma, patients can have detectable thyroglobulin levels, biochemical evidence of persistent disease, without visible disease by imaging studies (ultrasound, CT scanning, MRI, PET scanning). In some cases, it may represent residual normal thyroid tissue and be completely benign; however, this conclusion should only be made after adequate evaluation. Surgery, repeat radioactive iodine treatment or observation (in some cases) is done as clinically indicated. This low level of disease burden does not impact short-term risk and does not cause incapacitation; therefore, unless there are other indications for grounding, aviators may remain on flying status during the evaluations.

Thyroxine therapy is needed in all patients. Higher risk individuals with differentiated thyroid cancers are treated at doses sufficient to suppress the TSH and render the patient mildly thyrotoxic.

#### IV. Aeromedical Concerns.

Differentiated thyroid cancer poses little aeromedical risk unless there are distant metastases. Fortunately, only 10% of patients develop distant metastases over their life-time, and the majority are seen in the lungs. Bone and CNS metastases are even rarer. The tumors are slow growing in most cases. Even if residual disease is documented, the short-term risks are unchanged unless distant metastases are apparent. The aeromedical concerns center on post-operative and treatment complications. Post-surgical complications include hypothyroidism, and the small risk of damage to the recurrent laryngeal nerves and parathyroid glands due to local invasion, or surgical damage. Hypothyroidism is easily treated with thyroxine replacement; however, there may be times when replacement is deliberately withheld as part of treatment with the goal of inducing hypothyroidism for radioactive iodine scanning or treatment. Hypothyroid aviators should not be flying and should be placed in a DNIF status even if they have a waiver. Since TSH can stimulate tumor growth and TSH suppression can avoid this, appropriate suppressive therapy typically induces a degree of subclinical hyperthyroidism. The mild thyrotoxicosis slightly increases the risk of atrial fibrillation, but is not associated with sudden incapacitation and would not limit aviation duties.

In patients with thyroid cancer, surgery can lead to damage to the parathyroid glands resulting in permanent hypoparathyroidism causing hypocalcemia which can lead to tingling and muscle cramping or potentially life-threatening tetany. With proper treatment, this will be a waiverable condition for any flying class. It is easily treated with calcium and sometimes requires calcitriol, but most patients never have a problem as long as they are taking their pills. Symptoms of hypocalcemia are easily recognizable and reversible with calcium, long before a life-threatening event like tetany would occur. Likewise any lesion of the recurrent laryngeal nerve, whether iatrogenic or part of the natural disease process, would have further potential aeromedical implications. Unilateral involvement would likely result in increased vocal hoarseness which may affect the aviators ability to effectively communicate; particularly in an environment with significant levels of ambient noise. Bilateral damage may result in aphonia which would not be considered waiverable. Unilateral damage should be considered on a case-by-case basis, but bilateral damage is not a waiverable condition.

Medullary thyroid cancer can be an indolent process depending on the extent of the initial tumor. The treatment is aggressive surgical resection. Thus, the same post-operative considerations exist as for the differentiated thyroid carcinomas. Since local invasion is the primary risk; aeromedical concerns center on local damage or risks for future invasion or recurrence. Waiver can be

considered if there is no evidence of residual disease and no significant post-operative complications besides the expected hypothyroidism. Waiver can also be considered for those with only biochemical evidence of persistent disease with negative imaging, on a case by case basis, to include the small number with stable persistent disease with positive imaging, but not bad enough to require surgery.

As all anaplastic thyroid cancer is considered Stage IV, this diagnosis would not be considered waiverable.

| ICD9 Code for Thyroid Cancer |                                     |
|------------------------------|-------------------------------------|
| 193                          | Malignant neoplasm of thyroid gland |

| ICD10 Code for Thyroid Cancer |                                     |
|-------------------------------|-------------------------------------|
| C73                           | Malignant neoplasm of thyroid gland |

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### **Transient Ischemic Attack and Stroke (Mar 2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Updated Waiver Considerations, Table 1, Aeromedical Concerns and References

#### I. Waiver Consideration

Irrespective of etiology, stroke and TIA are disqualifying for all flying classes. Waivers are generally not considered unless a correctable cause is discovered and treated. Examples of correctable etiologies might include iatrogenically-induced stroke from catheterization or trauma to the carotid artery without residual injury, and repair of a large patent foramen ovale with intracardiac shunting. Modifiable vascular disease risk factors such as hypertension and hyperlipidemia are not considered correctable etiologies. Additionally, supratentorial strokes leave a potential seizure focus. A 2-3 year seizure-free observation period after stroke and a 1-2 year observation period after TIA are required prior to any potential waiver consideration. Any manned-aircraft pilot waiver recommendations after stroke or TIA are almost invariably limited to non high-performance, multi-crew platforms, often with further restriction of another fully trained pilot to be present during aircraft operation. Stroke is a dynamic field, with evolving evaluation and management guidance.

Table 1: Waiver potential for stroke and TIA

| Flying Class (FC) | Waiver Potential      | Waiver Authority | ACS Review or Evaluation |
|-------------------|-----------------------|------------------|--------------------------|
| FC I/IA           | Possibly <sup>1</sup> | AFMRA            | Yes                      |
| FC II//III/SWA    | Yes <sup>2</sup>      | AFMRA            | Yes                      |
| ATC/GBO           | Yes <sup>2</sup>      | AFMRA            | Yes                      |

<sup>1.</sup> Waiver recommendation may be considered in exceptional cases if felt secondary to a (treated) correctable cause, and with a suitable observation period

#### II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

### A. Initial Waiver Request:

- 1. History details of the incident to include the extent of symptoms, physical findings, timing of onset and resolution, and possible precipitating factors (i.e., Valsalva or +Gz preceding symptom onset).
- 2. Reports of consultations and diagnostic testing, including: neurology consultation, imaging studies (reports and images), laboratory testing, cardiac testing (ECG, echocardiogram (report and images), rhythm monitoring), and operative reports if applicable. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.

<sup>2.</sup> Must be 2-3 years post-stroke or 1-2 years post-TIA with no symptoms or clinically-insignificant residua

- 3. Current physical, mental status and neurologic examination findings.
- 4. Neuropsychological testing for all stroke cases. Contact ACS Neuropsychology for questions or further guidance on specific tests to administer.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical and neurologic exam findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual neurologic or cognitive symptoms and signs and any medication effects, on operational safety and mission effectiveness, future risk of recurrence, and future risk of seizures. Literature reports indicate stroke recurrence rate is highest immediately following the initial stroke and continues to remain aeromedically-unacceptably high indefinitely, up to 3-4% annually. However, these rates listed in the literature may overestimate the risk in USAF aviators, as many patients in these studies had significant, sometimes multiple vascular risk factors that are not present in the USAF aviator cohort. Also, strokes with a welldefined and correctable etiology, as well as cryptogenic strokes, may have an aeromedicallyacceptable lower incidence of recurrence and potentially amenable to waiver consideration. The role and management of patent foramen ovale in stroke is evanescent. Current guidelines advise closure in cases of large openings, recurrent vascular events, or with associated atrial septal aneurysm. Prolonged implantable cardiac monitoring to assess for occult atrial arrhythmias should be obtained in cases of cryptogenic stroke. Trans-esophageal echocardiography should also be considered in cryptogenic stroke cases to more thoroughly assess left atrial anatomy. The recentlycharacterized designation of Embolic Stroke of Undetermined Source (ESUS) consists of nonlacunar cryptogenic strokes with likely embolic etiology. Unfortunately, recurrence risk of ESUS is estimated at over 4% annually, and such aviators may not be recommend for aeromedical waiver. Also, atrial fibrillation-associated stroke may have an unacceptably-high recurrence risk for aeromedical waiver consideration. The risk of post-stroke seizures is aeromedically-unacceptably high for at least the first several years following a supratentorial stroke. Supratentorial cortical locations are associated with a higher seizure risk, but seizures also occur following subcortical lacunar strokes. The incidence of new-onset seizures declines over time, with population studies suggesting the risk becomes aeromedically-acceptable after 2-3 years.

Review of AIMWTS through Jan 2019 showed 45 cases of TIA/stroke; 17 were disqualified. Breakdown of the cases revealed: 28 FC II (10 disqualified), 2 RPA pilots (0 disqualified), 12 FC III (6 disqualified), and 3 MOD (1 disqualified).

| ICD-9 Code | ICD-9 Codes for transient ischemic attack and stroke |  |  |
|------------|--|--|--|
| 435.9      | Transient cerebral ischemia                          |  |  |
| 434.0      | Cerebral thrombosis                                  |  |  |
| 434.1      | Cerebral embolism                                    |  |  |
| 434.9      | Cerebral artery occlusion, unspecified               |  |  |
| 432.9      | Unspecified intracranial hemorrhage                  |  |  |
| 443.21     | Dissection of carotid artery                         |  |  |
| 443.24     | Dissection of vertebral artery                       |  |  |

| ICD-10 Codes for transient ischemic attack and stroke |   |  |
|---|---|--|
| G45.9   | Transient cerebral ischemia attack, unspecified                         |  |
| I63.00  | Cerebral infraction due to thrombosis of unspecified precerebral artery |  |
| I63.19  | Cerebral infarction due to embolism of other precerebral artery         |  |
| I66.9   | Occlusion and stenosis of unspecified cerebral artery                   |  |
| I62.9   | Nontraumatic intracranial hemorrhage, unspecified                       |  |
| I77.71  | Dissection of carotid artery  |  |
| I77.74  | Dissection of vertebral artery  |  |

### **IV. Suggested Readings**

- 1. Caplan LR. Overview of the evaluation of stroke. UpToDate, Jan 2, 2020.
- 2. Furie KL, Rost NS. Overview of secondary prevention of ischemic stroke. UpToDate, Jan 14, 2020.
- 3. Wang JZ et al. Incidence and management of seizures after ischemic stroke. Systemic review and meta-analysis. Neurology 2017; 89:1220-1228.
- 4. Edwardson MA. Ischemic stroke prognosis in adults. UpToDate, Jul 12, 2019.
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- 7. Yaghi S, Kamel H, Elkind MSV. Atrial cardiopathy: a mechanism of cryptogenic stroke. Extert Rev Cardiovasc Ther 2017; 15(8):591-599.
- 8. Hart RG et al. Embolic stroke of undetermined source: a systematic review and clinical update. Stroke 2017; 48:867-872.
- 9. Messé SR et al. Practice advisory: recurrent stroke with patent foramen ovale (update of practice parameter). Neurology 2016; 87(8):815-821.
- 10. Ropper AH, Samuels MA, Klein JP (Ed). Cerebrovascular disorders. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:778-884.
- 11. Meschia JL, Bushnell C, Boden-Albala B, et al. Guidelines for the Primary Prevention of Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke, 2014; 45: 3754-3832.
- 12. Prabhakaran S, Chong JY. Risk Factor Management for Stroke Prevention. American Academy of Neurology. Continuum (Minneap Minn) 2014; 20(2):296–308.

### **Traumatic Brain Injury (Mar 2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

### **Significant Changes:**

Updated Waiver Consideration, Tables and References

#### I. Waiver Consideration

Traumatic brain injury (TBI) unfortunately occurs too commonly in aviators. A history of TBI is generally disqualifying for all flying classes. Each TBI case has unique characteristics, and waiver consideration is on an individual basis, taking into account all factors. This individual variability makes it quite challenging to comprehensively address TBI in guidance tables. Severity classification is based on the 2007 DoD guidance with additional incorporation of clinical and radiographic information. Recommended post-injury observation periods are evidence-based to allow post-injury seizure risk to become aeromedically-acceptable for waiver consideration. Head injuries without significant sequelae are not disqualifying for OSF personnel per the Medical Standards Directory.

Following discussion with Career Field Managers, the Aeromedical Standards Working Group established a difference in acceptable risk for sudden incapacitation for selected enlisted aircrew and GBO personnel based on AFSC, allowing potential for earlier return to fly following aeromedically-moderate or severe head injury. Table 4 below lists this guidance.

Please contact ACS Neurology and/or Neuropsychology for any case-specific questions.

Table 1: Waiver potential for TBI

| Flying Class (FC) | Waiver Potential | Waiver Authority   | ACS Review or Evaluation                      |
|-------------------|------------------|--------------------|---|
| FC I/IA           | Yes              | AFMRA              | For moderate or severe TBI cases <sup>1</sup> |
| FC II/III/SWA     | Yes              | AFMRA <sup>2</sup> | For moderate or severe TBI cases <sup>1</sup> |
| ATC/GBO           | Yes              | AFMRA <sup>2</sup> | For moderate or severe TBI cases <sup>3</sup> |

- 1. ACS review/evaluation of mild head injury cases on request from the waiver authority
- 2. AETC is waiver authority for IFC II/III, I-GBO, I-SWA, and I-ATC cases.
- 3. No waiver required for uncomplicated ATC/GBO cases of aeromedically-mild TBI with normal examination

# II. Information Required for Waiver Submittal

Table 2 applies to head injuries that occurred less than five years from time of waiver request.

Table 2: Aeromedical Classification and Evaluation of TBIs less than five years from time of

waiver request.

| Degree of Head Injury       | Minimum            | Evaluation Requirements  |
|-----------------------------|--------------------|--|
| Degree of fieud injury      | Observation        | Evaluation Requirements  |
|                             | Time               |  |
| Aeromedical Mild            | 1 month            | Flying Class I, IA, II, III, RPA, SWA:                                       |
| (LOC or amnesia < 30        | 1 month            | Neurological exam: Complete neurological and mental                          |
| minutes; normal MRI)        |                    | status examination by a Flight Surgeon                                       |
|                             |                    | Imaging: noncontrast MRI   |
|                             |                    | Cognitive Assessment: Clinical interview and screening                       |
|                             |                    | (Montreal Cognitive Assessment or equivalent)                                |
| Aeromedical Moderate        | 6 months           | Flying Class I, IA, II, III, RPA, ATC, GBO, SWA:                             |
| (LOC or amnesia > 30        |                    | Neurological exam: Complete neurological and mental                          |
| minutes but < 24 hours      |                    | status examination by a Neurologist  |
| or non-displaced skull      |                    | <b>EEG</b> : obtain locally if any seizure activity                          |
| fracture; normal MRI)       |                    | reported/observed  |
| ,                           |                    | Imaging: noncontrast MRI   |
|                             |                    | Neuropsychological evaluation: Local, to include                             |
|                             |                    | assessment of general cognitive functioning and major                        |
|                             |                    | cognitive domains. Contact ACS Neuropsychology for                           |
|                             |                    | guidance on specific testing. Include any test scores with                   |
|                             |                    | waiver package   |
| <b>Aeromedical Moderate</b> | 2 years            | Flying Class I, IA, II, III <sup>1</sup> , RPA, ATC, GBO <sup>1</sup> , SWA: |
| (LOC or amnesia > 30        | for most           | Neurological exam: Complete neurological and mental                          |
| minutes but < 24 hours      | AFSCs,             | status examination by a Neurologist  |
| or non-displaced skull      | 6 months           | <b>EEG</b> : obtain locally if any seizure activity                          |
| fracture; MRI               | for specific       | reported/observed  |
| demonstrating               | AFSCs <sup>1</sup> | <b>Imaging</b> : noncontrast MRI locally within one month of                 |
| evidence of diffuse         |                    | injury; follow-up MRI at time of waiver submission                           |
| axonal injury or            |                    | <b>Neuropsychological evaluation</b> : A local NP evaluation                 |
| hemosiderin                 |                    | during the 3-9 month post-TBI period, to include                             |
| deposition/plugs)           |                    | assessment of general cognitive functioning and major                        |
|                             |                    | cognitive domains. Contact ACS Neuropsychology for                           |
|                             |                    | guidance on specific testing. Include any test scores with                   |
|                             |                    | waiver package   |
| Aeromedical Severe          | 2 years            | Flying Class I, IA, II, III, RPA, ATC, GBO, SWA:                             |
| (LOC or amnesia > 24        |                    | Neurological exam: Complete neurological and mental                          |
| hours; normal MRI or        |                    | status examination by a Neurologist  |
| MRI demonstrating           |                    | EEG: locally or during ACS evaluation  |
| inconsequential             |                    | Imaging: noncontrast MRI locally within one month of                         |
| hemorrhage or               |                    | injury; follow-up MRI at time of waiver submission                           |
| evidence of diffuse         |                    | Neuropsychological evaluation: A local NP evaluation                         |
| axonal injury or            |                    | during the 3-9 month post-TBI period, to include                             |

| hemosiderin<br>deposition/plugs)  |  | assessment of general cognitive functioning and major cognitive domains. Contact ACS Neuropsychology for guidance on specific testing. Include any test scores with waiver package   |
|---|--|--|
| Aeromedical Severe<br>(LOC or amnesia > 24<br>hours; presence of<br>subdural hematoma or<br>brain contusion; MRI<br>demonstrating more<br>significant<br>abnormalities) | 5 years<br>for most<br>AFSCs,<br>2 years for<br>specific<br>AFSCs <sup>1</sup> | Flying Class I, IA, II, III¹, RPA, ATC, GBO¹, SWA: ACS: evaluation Neurological exam: Complete neurological and mental status examination by a Neurologist EEG: locally or during ACS evaluation. Imaging: noncontrast MRI locally within one month of injury; follow-up MRI at time of waiver submission Neuropsychological evaluation: A local NP evaluation during the 3-9 month post-TBI period, to include assessment of general cognitive functioning and major cognitive domains. Contact ACS Neuropsychology for guidance on specific testing. Include any test scores with waiver package |
| Aeromedical Severe<br>(penetrating injury,<br>volume loss > 25cc, late<br>seizure, shunt,<br>significant deficits)  | No waiver possible   | All Flying Classes   |

<sup>1.</sup> FC III and GBO AFSCs that may be considered for waiver for moderate head injury at 6 months, or for waiver for severe head injury at 2 years, are listed in Table 4.

Table 3 applies to IFC applicants with a remote history of TBI, defined as five years or more postinjury.

Table 3: IFC applicants (all classes) with history of remote (>=5 years) TBI

| Table 3: IFC applicants (all classes) with history of remote (>=5 years) TBI |  |  |  |
|--|--|--|--|
| Normal exam and imaging at time of injury                                    | Neurological exam: Complete neurological             |  |  |
|  | and mental status examination by a Flight            |  |  |
|  | Surgeon  |  |  |
|  | <b>Imaging</b> : report and images of prior studies. |  |  |
|  | Current non-contrast brain MRI if no prior           |  |  |
|  | MRI was performed                                    |  |  |
|  | Neuropsychological evaluation: not required          |  |  |
|  | unless felt clinically indicated by the Flight       |  |  |
|  | Surgeon  |  |  |
|  | <b>Review</b> : AETC/SGP. ACS review at discretion   |  |  |
|  | of waiver authority                                  |  |  |
| Abnormal exam, imaging or EEG at time of                                     | Neurological exam: Complete neurological             |  |  |
| injury   | and mental status examination by a Flight            |  |  |
|  | Surgeon  |  |  |
|  | <b>Imaging</b> : report and images of prior studies. |  |  |
|  | Current non-contrast brain MRI if no follow-         |  |  |
|  | up neuroimaging was performed                        |  |  |
|  | <b>EEG</b> : report of previous studies.             |  |  |
|  | Current sleep-deprived EEG if any previous           |  |  |
|  | EEG study was reported as abnormal                   |  |  |
|  | Neuropsychological evaluation: not required          |  |  |
|  | unless felt clinically indicated by the Flight       |  |  |
|  | Surgeon  |  |  |
|  | <b>Review</b> : AETC/SGP. ACS review at discretion   |  |  |
|  | of waiver authority                                  |  |  |
| Seizure within 24 hours of time of injury <sup>1</sup>                       | Neurological exam: Complete neurological             |  |  |
|  | and mental status examination by a Flight            |  |  |
|  | Surgeon  |  |  |
|  | <b>Imaging</b> : report and images of prior studies. |  |  |
|  | Current non-contrast brain MRI if no follow-         |  |  |
|  | up neuroimaging was performed                        |  |  |
|  | <b>EEG</b> : report of previous studies.             |  |  |
|  | Current sleep-deprived EEG if no previous            |  |  |
|  | studies were performed or if any previous EEG        |  |  |
|  | study was reported as abnormal                       |  |  |
|  | Neuropsychological evaluation: not required          |  |  |
|  | unless felt clinically indicated by the Flight       |  |  |
|  | Surgeon  |  |  |
|  | <b>Review</b> : AETC/SGP. ACS review at discretion   |  |  |
|  | of waiver authority                                  |  |  |

of waiver authority

1. Seizures occurring 24 hours or later following TBI are disqualifying. In such cases, please refer to the Seizures/Epilepsy/Abnormal EEG Waiver Guide chapter for further information.

Table 4 lists FC III and GBO AFSCs that can be considered for <u>earlier</u> TBI waiver (6 months for moderate and 2 years for severe injury).

Table 4: Specific AFSCs that qualify for earlier TBI waiver consideration

| 1A2X1 | Aircraft Loadmaster                       |
|-------|---|
| 1A3X1 | Airborne Mission Systems                  |
| 1A4X1 | Airborne Operations                       |
| 1A6X1 | Flight Attendant                          |
| 1A8X1 | Airborne Cryptologic Language Analyst     |
| 1A8X2 | Airborne ISR Operator                     |
| 1B4X1 | Cyberspace Defense Operations             |
| 1C6X1 | Space Systems Operations                  |
| 1T0X1 | Survival, Evasion, Resistance, and Escape |
| 1T2X1 | Pararescue                                |
| 13BX  | Air Battle Manager                        |
| 13LX  | Air Liaison Officer                       |
| 13SX  | Space & Missile                           |
| 17DX  | Cyberspace Operations                     |

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

# A. <u>Initial Waiver Request:</u>

- 1. Historical details of the injury and initial treatment. Include clinical notes from initial evaluation and treatment.
- 2. Evaluation as outlined in Tables 2 and 3 above. Include reports of consultations and diagnostic testing, including: neurology consultations, neuroimaging studies (e.g. MRI reports and images), laboratory testing, any operative reports and EEG reports. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Current physical, mental status and neurologic examination findings.
- 4. Neuropsychological testing results (if performed). Contact ACS Neuropsychology for questions or further guidance on need for testing and on which tests to administer.
- 5. RILO/MEB results, if obtained.
- 6. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1 Interval history and level of symptom resolution.
- 2 Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3 Current physical, mental status and neurologic examination findings.
- 4 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Aeromedical concerns include effects of any residual neurologic or cognitive symptoms and signs and any medication effects on operational safety and mission effectiveness, and future risk of seizure with resulting sudden incapacitation. The risk to safety of flight from a fixed neurological deficit is readily apparent. Cognitive deficits may not be readily apparent but can be assessed with appropriate testing. Military aviation stressors such as hypoxia, high +G exposure and sleep disruption may precipitate seizures. Anticonvulsant medications are not currently approved for use in aviators for seizure prophylaxis, primarily due to their central-acting effects on cognition and alertness, and secondarily for the potential of withdrawal seizures following abrupt discontinuation. Interestingly, immediate and early (7 days or less) post-traumatic seizures do not produce an increased future seizure risk, while seizures occurring over 7 days post-TBI do. Annegers' seminal studies indicated the relative risk of seizures following even mild TBI compared to the normal population remains elevated for five years, while the relative risk after moderate or severe TBI remains elevated for over ten years. The actual incidence of seizures, however, becomes aeromedically acceptable much sooner, reflected in recommended observation periods listed in Table 2 above. In one study of USAF aircrew who met waiver criteria, seizures occurred at a rate of 24.53/100,000 person-years. A retrospective study of Vietnam War veterans with penetrating TBIs noted posttraumatic epilepsy in 53% at 15-years; of these 7% experienced their first seizure more than ten years following their trauma. A 0-25 cc volume loss was associated with a 42% seizure incidence while loss > 75 cc was associated with an incidence of 80%. Other imaging findings that increase post-traumatic seizure risk include subdural hematoma, contusions, microhemorrhages and blood breakdown product deposition. As noted earlier, every TBI case is unique, and all information must be taken into consideration when determining aeromedical waiver suitability.

AIMWTS search in Jan 2019 revealed 1337 individuals with a waiver that contained a diagnosis of closed head injury. The breakdown of cases was as follows: 342 FC I/1IA (38 disqualifications), 308 FC II (16 disqualifications), 17 RPA pilot cases, 592 FC III (83 disqualifications), 48 ATC/GBC (11 disqualifications), and 30 MOD (6 disqualifications). There were 154 cases resulting in a disposition of disqualify, and in well over half of the cases the major reason for the disqualification was the head injury.

| ICD-9 codes for traumatic brain injury |  |  |  |
|--|--|--|--|
| 800-801                                | Skull fracture   |  |  |
| 850.1                                  | Concussion with brief loss of consciousness                              |  |  |
| 854.01                                 | Intracranial injury of other and unspecified nature without open         |  |  |
|  | intracranial wound with no loss of consciousness                         |  |  |
| 854.02                                 | Intracranial injury of other and unspecified nature without open         |  |  |
|  | intracranial wound with brief (less than one hour) loss of consciousness |  |  |
| 854.03                                 | Intracranial injury of other and unspecified nature without open         |  |  |
|  | intracranial wound with moderate (1-24 hours) loss of consciousness      |  |  |
| 959.01                                 | Head injury, unspecified   |  |  |

| ICD-10 codes | ICD-10 codes for traumatic brain injury                                   |  |  |
|--------------|---|--|--|
| S02.0        | Fracture of vault of the skull, closed                                    |  |  |
| S06.0X1      | Concussion with loss of consciousness of 30 minutes or less               |  |  |
| S06.0X2      |   |  |  |
| S06.890      | Other specified intracranial injury without loss of consciousness         |  |  |
| S06.9X1      | Unspecified intracranial injury with loss of consciousness of 30 minutes  |  |  |
|              | or less   |  |  |
| S06.9X2      | Unspecified intracranial injury with loss of consciousness of 31 minutes  |  |  |
|              | to 59 minutes   |  |  |
| S06.9X3      | Unspecified intracranial injury with loss of consciousness of 1 hour to 5 |  |  |
|              | hours 59 minutes  |  |  |
| S06.9X4      | Unspecified intracranial injury with loss of consciousness of 6 hours to  |  |  |
|              | 24 hours  |  |  |
| S09.80       | Unspecified injury of head  |  |  |

# IV. Suggested Readings

- 1. Evans RW, Whitlow CT. Acute mild traumatic brain injury (concussion) in adults. UpToDate, Mar 8, 2019.
- 2. Rajajee V. Management of acute moderate and severe traumatic brain injury. UpToDate, Dec 23, 2019.
- 3. Christensen J. The epidemiology of posttraumatic epilepsy. Semin Neurol 2015; 35:218-222
- 4. Ropper AH, Samuels MA, Klein JP (Ed). Craniocerebral trauma. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:885-914.
- 5. McGuire SA et al. Aeromedical decision making and seizure risk after traumatic brain injury: longitudinal outcome. Aviat Space Environ Med 2012; 83(2):140-43.
- 6. Christensen JC et al. Long-term risk of epilepsy after traumatic brain injury in children and young adults: a population-based study. Lancet 2009; 373:1105-1110.
- 7. Agrawal A et al. Post-traumatic epilepsy: an overview. Clinical Neurology and Neurosurgery 2006; 108:433-439.
- 8. Annegers J, Coan S. The risks of epilepsy after traumatic brain injury. Seizure 2000; 9:453-457.
- 9. Annegers JF et al. A population-based study of seizures after traumatic brain injuries. N Engl J Med 1998; 338:20-24.
- 10. Salazar AM, Jabbari B, Vance SC, et al. Epilepsy after penetrating head injury. I. Clinical correlates: A report of the Vietnam Head Injury Study. Neurology 1985; 35: 1406-14.

## **Ulcerative Colitis (Apr 2019)**

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

**Significant Changes:** Waiver guide updated to reflect national guidelines, waiver requirements updated, career field-specific approved medications clarified, and aeromedical concerns section expanded

### I. Waiver Consideration

Ulcerative Colitis (UC) of any severity or distribution is disqualifying for all flying classes, ground-based operators, and other special duty operators as well as for retention. Included in this diagnosis are proctitis, disease limited to the left side of the colon, and extensive (pancolonic) disease. Aeromedical waiver is usually not recommended for untrained personnel. Factors considered when assessing suitability for aeromedical waiver include the severity of disease at diagnosis, evidence of clinical and endoscopic remission, whether treatment and monitoring are appropriate in the context of nationally or internationally recognized guidelines, the risk associated with specific medication(s), the individual service member's tolerance of the medication(s) and adherence to therapy, and the cumulative risk of all associated complications and/or extra-intestinal manifestations. Individuals not on an appropriate treatment regimen will not be considered waiver-eligible. Waiver can be considered once an aviator is in disease remission on a stable, aeromedically-approved medication regimen, without adverse effects. Use of any medication not included on the career field-specific approved medication list is independently disqualifying and will be considered on a case-by-case basis.

Individuals who demonstrate clinical but not endoscopic remission will not be considered waivereligible due to studies that show a higher risk for symptomatic recurrence when there is persistent disease on endoscopy. For aeromedical purposes, endoscopic remission is assessed either after completion of treatment or while on maintenance therapy and is defined as visual (i.e., colonoscopic) and histologic (i.e., tissue biopsy) demonstration of mucosal healing without evidence of active inflammation. Finally, aeromedical waivers for UC treated with curative surgeries are considered on a case-by-case basis, with aeromedical consideration given to postoperative complications and functional outcomes.

Table 1: Waiver potential for Ulcerative Colitis including proctitis, left-sided disease, and extensive disease

| Flying Class (FC)   | Condition  | Waiver Potential <sup>1</sup> Waiver Authority | ACS Review or Evaluation |
|---------------------|--|--|--------------------------|
| I/IA                | Ulcerative colitis of any degree                       | No<br>AETC                                     | N/A                      |
| II//III/<br>GBO/ATC | Ulcerative colitis of any degree <sup>2,3,4</sup>      | Yes<br>MAJCOM                                  | Yes                      |
| SWA                 | Ulcerative colitis treated with colectomy <sup>5</sup> | Yes<br>MAJCOM                                  | Yes                      |

- 1 Untrained personnel of any class are unlikely to receive aeromedical waiver, and ACS review/evaluation is not necessary.
- Waiver consideration is based on clinical remission, endoscopic remission, appropriateness of therapy, and whether disease remission can be maintained with career field-specific approved medications. Use of any medication not included on the career field-specific approved medication list is independently disqualifying and will be considered on a case-by-case basis (see section III. Aeromedical Concerns).
- 3 Clinical and endoscopic remission is required prior to waiver consideration. For aeromedical purposes, endoscopic remission is assessed either after completion of treatment or while on maintenance therapy and is defined as visual (i.e., colonoscopic) and histologic (i.e., tissue biopsy) demonstration of mucosal healing without any evidence of active inflammation.
- 4 Individuals treated with TNF-alpha inhibitors will be considered for a restricted waiver (not worldwide qualified, TDY requires access to transport, and refrigeration of medication) if found fit for military retention, and waiver authority is AFMRA.
- 5 Aeromedical waivers after curative surgeries are considered on a case-by-case basis, with aeromedical consideration given to post-operative complications and functional outcomes.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# A. <u>Initial Waiver Request:</u>

- 1. Summary of presentation, course, and treatment.
- 2. Consultation reports from all treating providers or specialists, which should include:
  - a. Subjective symptoms and objective physical exam findings.
  - b. Current treatment plan, to include tolerance and current doses of maintenance medications and all appropriate monitoring labs for those medications, as applicable (e.g., biologic agents require CBC/CMP every 3-6 months and annual TB testing).
  - c. Documentation excluding/including extra-intestinal manifestations (e.g., ankylosing spondylitis, anterior uveitis, primary sclerosing cholangitis, etc.).
- 3. Results of all pertinent laboratory studies, including diagnostic and follow-up results. Must include recent CBC, CMP, ESR, and CRP.
- 4. Radiology reports from all diagnostic or follow-up imaging studies.
- 5. All endoscopy and biopsy reports, including results of repeat endoscopy while clinically stable demonstrating endoscopic remission.
- 6. Current physical examination findings.
- 7. FL4 with RTD and ALC status.

- 8. Any other pertinent information.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Current symptoms and development of any disease flares, complications, or extraintestinal manifestations.
  - b. Current medications, doses, and adverse effects.
  - c. Current physical examination findings.
- 2 Consultation reports from treating gastroenterologist or internist.
- 3 Any interval endoscopy reports with biopsy results.
- 4 Updated CBC, CMP, ESR, and CRP.
- 5 Any other pertinent information.
- 6 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## **III. Aeromedical Concerns**

Ulcerative colitis is a chronic, relapsing and remitting inflammatory disease primarily affecting the colon in a contiguous pattern, usually beginning in the rectum. Depending on the extent of colonic involvement, the disease is subdivided into proctitis, left-sided disease, and extensive disease. Assessments of disease severity are based on multiple factors, including the number of daily bowel movements, presence or absence of hematochezia, levels of serum inflammatory markers, endoscopic findings, and signs of systemic toxicity (e.g., tachycardia, hypotension, fever, anemia, etc.). Disease severity is then typically reported as mild-to-moderate or moderate-to-severe. Uncontrolled or untreated UC can result in distracting symptoms such as frequent diarrhea, abdominal pain, weight loss, and fatigue. Chronic blood loss or underlying inflammation may lead to aeromedically significant iron deficiency anemia or anemia of chronic disease, respectively. Recurrent or persistent colonic inflammation in UC increases the risk of dysplasia and colon cancer. All individuals with UC should undergo careful assessment for extra-intestinal manifestations of the disease, including anterior uveitis, primary sclerosing cholangitis, and inflammatory arthritis. Remission can occur spontaneously, but most individuals with UC will require maintenance medications to maintain disease control. Symptomatic and endoscopic remission is required prior to waiver submission, whether spontaneous or as a result of maintenance treatment with career field approved medications. Once clinical remission is achieved, endoscopic remission must be confirmed prior to waiver consideration. Although repeat endoscopy to assess for mucosal healing is not always performed in clinical practice, the risk of disease flare or long-term complication is increased in individuals who do not achieve endoscopic remission, despite absence of symptoms.

Treatment for UC is primarily directed toward the induction and maintenance of remission. In mild-to-moderate disease, 5-aminosalicylates are first line therapy. There are several 5-aminosalicylate formulations that are approved for use in aviation, ground-based, and special duty operations. To induce and maintain remission in moderate-to-severe disease, more aggressive forms of therapy are usually required, such as oral steroids, immunomodulators, or biologic agents. Currently, only two biologic agents (infliximab and adalimumab) are approved for aviation, ground-based, and special duty operations. Oral steroids and immunomodulators such as azathioprine and 6-mercaptopurine

are not currently approved for use due to the unacceptable adverse effect profile and/or need for frequent laboratory monitoring. However, azathioprine and 6-mercaptopurine are increasingly being used to induce and maintain remission in UC. The most concerning aeromedical adverse effects of these medications are the development of myelosuppresion, pancreatitis, and/or hepatotoxicity. The highest risk for severe myelosuppression occurs within the first year of therapy. Thiopurine methyltrasnferase (TPMT) genotype testing is required prior to initiating these medications to identify a subset of individuals at high risk of developing severe myelosuppression. In certain low-risk unmanned aviators or ground-based operators, azathioprine and 6-mercatopurine could be considered for waiver on a case-by-case basis.

About 10 to 15% of individuals with ulcerative colitis require a partial or total colectomy. Often, these resections are curative, and maintenance therapy is no longer required. Provided that an individual is asymptomatic without surgical complication, ileostomy, or colostomy, an aeromedical waiver can be considered.

Individuals who received treatment with exogenous steroids for greater than three weeks within the last year require aeromedical assessment of the hypothalamic-pituitary-adrenal axis prior to waiver consideration. Please refer to the Systemic Glucocorticoid (Steroid) Treatment waiver guide.

Review of AIMWITS data in Apr 2019 revealed a total of 82 waiver packages containing the diagnosis of ulcerative colitis since Jan 2014. Of that total, 3 were FC I/IA (2 disqualified), 49 were FC II (3 disqualified), 23 were FC III (2 disqualified), 7 were ATC/GBC (1 disqualified), and 0 were MOD.

| ICD-9 codes for Ulcerative Colitis |                                 |  |
|------------------------------------|---------------------------------|--|
| 556.2                              | Ulcerative proctitits           |  |
| 556.9                              | Ulcerative colitis, unspecified |  |

| ICD-10 codes for Ulcerative Colitis |                                 |
|-------------------------------------|---------------------------------|
| K51.2                               | Ulcerative colitis proctitis    |
| K51.9                               | Ulcerative colitis, unspecified |

## IV. Suggested Readings

- 1. Magro F, Gionechetti P, Eliakim R, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery, and Ileo-anal Pouch Disorders. J Crohn's and Colitis, 2017; 11(6): 649-670. Available at <a href="https://www.ecco-ibd.eu/publications/ecco-guidelines-science/published-ecco-guidelines.html">https://www.ecco-ibd.eu/publications/ecco-guidelines.html</a>
- 2. Harbord M, Eliakim R, Benntnworth D, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. J Crohn's and Colitis, 2017; 11(7): 769-784. Available at <a href="https://www.ecco-ibd.eu/publications/ecco-guidelines-science/published-ecco-guidelines.html">https://www.ecco-ibd.eu/publications/ecco-guidelines-science/published-ecco-guidelines.html</a>

- 3. Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology, 2019; 156(3): 748-64. Available at <a href="https://www.gastro.org/guidelines/ibd-and-bowel-disorders">https://www.gastro.org/guidelines/ibd-and-bowel-disorders</a>
- 4. Kornbluth A, Sachar DB, et al. Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice parameters Committee. Am J Gastroenterol, 2010; 105: 501-23.
- 5. Fumery, Mathurin, et al. Natural History of Adult Ulcerative colitis in Population-based Cohorts: A Systemic Review. Clinical Gastroenterology and Hepatology. March 2018; 16(3):343-356.

# Urticaria, Angioedema, & Anaphylaxis (Apr 2019)

Authors/Reviewers: Dr. Christopher Keirns, Maj Laura Bridge, and Capt Luke Menner (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator); and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

**Significant Changes:** Waiver guide restructured. Waiver potential and restrictions updated. Table 1 updated.

## I. Waiver Consideration

Chronic urticaria, angioedema, and anaphylaxis are generally each disqualifying for all manned and unmanned flying classes in the US Air Force. Depending on the severity of symptoms and causative etiology, these conditions may also be disqualifying for other rated duties and/or for retention. When anaphylaxis is recurrent, it is generally considered disqualifying for all flying classes and special duties due to the systemic nature of the reaction. Likewise, angioedema is considered disqualifying for FC I, II, III and SWA duties due to the potential for severe episodes, which preclude safe performance of flying duties when untreated. A single episode of angioedema or urticaria that is unprovoked and resolves without complication does not necessarily require a waiver, although the aviator must remain DNIF until symptoms completely remit. Cross-referencing with the medical standards directory (MSD) is recommended in each individual case for specific applicability of aeromedical and special duty standards.

Acromedical waivers for chronic urticaria, angioedema, and/or anaphylaxis may be considered after ACS review for all flying classes and special duty operators, including both untrained and trained personnel. To be eligible for an aeromedical waiver, the member must undergo a comprehensive allergy evaluation to identify any potential inciting triggers. Waivers can often be considered if a treatable/avoidable cause is identified. Idiopathic urticaria, angioedema, and/or anaphylaxis can also be considered for waiver on a case-by-case basis if the member is on effective prophylaxis with an aeromedically-approved medication (e.g., second-generation antihistamine) and is asymptomatic for at least three months.

Once an individual meets waiver criteria and a case is referred to the ACS, waivers are considered on an individualized basis. (See "Information Required for Waiver Submittal"). Factors that are weighed include the historical severity/extent of symptoms, the treatments required to resolve/control symptoms, and the frequency of episodes. Aeromedical risk is considered to be lower in those aviators who react to an identifiable and avoidable allergic trigger. The need for an EpiPen may not be compatible with unrestricted flying duties and could result in a IIC restriction for pilots (multiplace aircraft with another qualified pilot).

Table 1: Waiver potential for urticaria, angioedema, and anaphylaxis<sup>1</sup>

| -                 | tential for urticaria, angloeder                   | Waiver Potential <sup>2</sup> ACS Review |            |
|-------------------|--|--|------------|
| Flying Class (FC) | Condition  | Waiver Authority                         | Evaluation |
| I/IA              | Chronic urticaria and/or                           | Yes                                      | Yes        |
|                   | angioedema   | AETC                                     |            |
|                   | Urticaria and/or angioedema                        | No                                       | No         |
|                   | that is chronic, severe, and not controllable with | MAJCOM                                   |            |
|                   | aeromedically/operationally-                       |  |            |
|                   | approved medications                               | Yes                                      | Yes        |
|                   |  | AETC                                     |            |
|                   | History of anaphylaxis                             |  |            |
| II/III            | Chronic urticaria and/or                           | Yes                                      | Yes        |
| SWA               | angioedema   | MAJCOM                                   |            |
|                   | Urticaria and/or angioedema                        | No                                       | No         |
|                   | that is chronic, severe, and not controllable with | MAJCOM                                   |            |
|                   | aeromedically/operationally-                       |  |            |
|                   | approved medications                               | Yes<br>MAJCOM                            | Yes        |
|                   | History of anaphylaxis                             |  |            |
| GBO               | Chronic urticaria and/or angioedema                | N/A                                      | N/A        |
|                   | Urticaria and/or angioedema                        | No                                       | No         |
|                   | that is chronic, severe, and                       | MAJCOM                                   |            |
|                   | not controllable with                              |  |            |
|                   | aeromedically/operationally-                       |  |            |
|                   | approved medications                               | Yes                                      | Yes        |
|                   |  | MAJCOM                                   |            |
|                   | History of anaphylaxis                             |  |            |

<sup>1.</sup> Indefinite waivers will not be granted.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
  - a. Describe episodes, including symptoms, duration, and frequency of events
  - b. List all treatments and their effectiveness
  - c. List exacerbating/triggering factors (if known)

<sup>2.</sup> If applicable, submit allergen immunotherapy waiver requests after maintenance phase has been reached.

- d. List any other atopic conditions (e.g., asthma, allergies, eczema, etc.)
- 2. Allergy consult result (including all diagnostic tests performed).
- 3. If on medication therapy for chronic <u>idiopathic</u> urticaria or angioedema, medications must be aeromedically approved and dosing must be stable for 3 months without disease recurrence.
- 4. If on immunotherapy, note from allergist describing ongoing treatment plan.
- 5. Current physical examination findings.
- 6. Any other pertinent information.
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

Note: Specify in the AMS any reasoning/justification for not including items listed above with the submitted waiver package.

# B. Renewal Waiver Request:

- 1 Updated AMS with interval history, including:
  - a. Any recurrences of symptoms
  - b. Any changes in medications
  - c. Updated clinical evaluation note from allergist or flight surgeon/PCM
- 2 If on immunotherapy, note from allergist describing ongoing treatment plan.
- 3 Current physical examination findings.
- 4 Any other pertinent information.
- 5 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

Note: Specify in the AMS any reasoning/justification for not including items listed above with the submitted waiver package.

## **III. Aeromedical Concerns**

The primary aeromedical concerns for aviators with a history of chronic or recurrent urticaria, angioedema, or anaphylaxis relate to the risk that a subsequent event could result in sudden incapacitation or symptoms of sufficient severity to adversely affect performance, mission, and safety. In most cases, the risk of sudden incapacitation and death is presumed to be highest for those individuals with a history of anaphylaxis. When untreated, anaphylaxis can result in airway compromise and/or cardiovascular collapse in less than five minutes. The severity of a recurrence cannot be reliably predicted based on the extent/severity of symptoms during previous episodes. Of particular concern during flight, symptoms may return after an initial improvement or can persist for hours or days or, requiring further medical intervention to prevent systemic collapse.

Angioedema is commonly seen as a component of anaphylaxis or in co-occurrence with urticaria, but it can also occur independently. The risks and approaches to management differ with the underlying etiology. While an avoidable/allergic trigger can be identified in some cases, the cause of chronic angioedema or urticaria is often idiopathic. Recurrences can be unpredictable, and in some cases, symptoms are provoked by physical or emotional stress, such as that experienced in the aviation environment. There is an associated risk of sudden incapacitation due to edema of the tissues of the tongue/pharynx and airway compromise. In the absence of anaphylaxis (i.e., a history

of multisystem involvement), the risk of sudden incapacitation is considered less. When swelling is limited to the face/cheeks, there remains a potential for progression without medical intervention. Even mild symptoms pose a risk for distraction and performance decrement, particularly during critical phases of flight. Facial swelling could interfere with the wearing of the aviator mask or other life support equipment, and periorbital swelling could obstruct the field of vision.

Chronic urticaria without angioedema is usually considered non-life threatening, but extensive involvement can result in distraction and performance decrement, particularly during critical phases of flight. If left untreated, symptoms can progress, and the possibility for the development of angioedema exists. Like angioedema, symptoms can be provoked by stress in some individuals. Of aeromedical significance, many of the medications used to treat or control chronic urticaria are sedating. Fortunately, there are two, second-generation antihistamines that are approved for use in USAF aircrew (fexofenadine and loratadine), which are often effective at maintaining remission when used daily. However, they are not aeromedically-approved for the treatment or prophylaxis of urticaria and/or angioedema, and utilization of them for this indication requires a waiver.

Review of AIMWTS data in Apr 2019 revealed a total of 75 waiver packages containing the diagnosis of urticaria since Jan 2014. Of that total, 6 were FC I/IA (0 disqualified), 36 were FC II (4 disqualified), 27 were FC III (4 disqualified), 6 were ATC/GBC (1 disqualified), and 0 were MOD.

Review of AIMWTS data in Apr 2019 revealed a total of 41 waiver packages containing the diagnosis of angioedema since Jan 2014. Of that total, 1 were FC I/IA (0 disqualified), 24 were FC II (2 disqualified), 13 were FC III (1 disqualified), 2 were ATC/GBC (0 disqualified), and 1 were MOD (0 disqualified).

Review of AIMWTS data in Apr 2019 revealed a total of 13 waiver packages containing the diagnosis of anaphylaxis since Jan 2014. Of that total, 0 were FC I/IA, 5 were FC II (0 disqualified), 7 were FC III (3 disqualified), 0 were ATC/GBC, and 1 were MOD (1 disqualified). Review of the cases revealed that there were numerous overlapping diagnoses in each category. The vast majority of all the disqualifications resulted from the diagnoses of urticaria, angioedema, or anaphylaxis.

| ICD-9 codes for urticaria, angioedema, anaphylaxis |   |  |  |  |
|--|---|--|--|--|
| 708  | Urticaria   |  |  |  |
| 995.1  | Angioedema  |  |  |  |
| 995.0  | Anaphylaxis unspecified                             |  |  |  |
| 995.6  | Anaphylaxis due to food                             |  |  |  |
| ICD-10 codes fo                                    | ICD-10 codes for urticaria, angioedema, anaphylaxis |  |  |  |
| L50  | Urticaria   |  |  |  |
| T78.3  | Angioedema  |  |  |  |
| T78.0  | Anaphylaxis due to food                             |  |  |  |
| T78.2  | Anaphylaxis unspecified                             |  |  |  |

## **IV. Suggested Readings**

1. Sánchez-Borges M, Asero R, Ansotegui IJ, et al. Diagnosis and treatment of urticaria and angioedema: a worldwide perspective. World Allergy Organ J 2012; 5:124-147.

- 2. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy 2014; 69:868-87.
- 3. Bernstein JA, Lang DM, Khan DA. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol 2014; 133:1270-1277.
- 4. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis a practice parameter update 2015. Ann Allergy Asthma Immunol 2015; 115:341-384.
- 5. Simons FER, Ebisawa M, Sánchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J 2015; 8:32. Available at https://doi.org/10.1186/s40413-015-0080-1.

## **Uterine Fibroids (Leiomyomas) (Feb 2019)**

Reviewed: Dr. Hattie McAviney (RAM 20), Dr. Dan Van Syoc (Deputy Chief, ACS), Lt Col Jason Massengill (AF/SG consultant for OB/GYN), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

None.

## I. Waiver Consideration

Asymptomatic fibroids are not disqualifying and as such, require no waiver. Abnormal uterine bleeding – leiomyoma or pelvic pain secondary to leiomyomas, however, are disqualifying for flying classes (FC) I/IA, II, III and SWA. The condition is not listed as disqualifying for ATC and GBO duties, nor is it disqualifying for retention purposes, but significant symptoms and/or treatments may require duty restriction or limitation based on the medication and clinical evaluation. The use of hormone suppressive medications such as oral contraceptive pills (OCPs), progesterone supplementation, or a progesterone containing intrauterine device do not require a waiver. The use of any hormonal suppressive therapy should be monitored for adverse effects and effectiveness in controlling symptoms as they relate to duty performance. The use of other medications such as GnRH agonists/antagonists, aromatase inhibitors, or similar medications requires a waiver due to their association with significant and unpredictable symptoms. Use of these medications also requires a trial period to assess tolerance before considering a waiver. A history of a surgical treatment for symptomatic benign fibroids, such as myomectomy, uterine artery embolization, or hysterectomy, if uncomplicated, fully recovered, and asymptomatic, does not require waiver for any flying class exam, however, the non-malignant histology should be documented. These patients are not required to have their cases reviewed by the ACS.

Table 1: Waiver potential for uterine fibroids

| Condition                 | Waiver Potential  |  |
|---------------------------|---|--|
|                           | Waiver Authority  |  |
| Medically treated with    | Maybe   |  |
| OCPs, progestin or NSAIDs | AETC  |  |
| Medically treated with    | No  |  |
| GnRH analog <sup>1</sup>  | AETC  |  |
| Medically treated with    | Yes   |  |
| OCPs, progestin or NSAIDs | MAJCOM  |  |
| Medically treated with    | No  |  |
| GnRH analog <sup>1</sup>  | MAJCOM  |  |
| Medically treated with    | Yes   |  |
| OCPs, progestin or NSAIDs | MAJCOM  |  |
| Medically treated with    | Maybe   |  |
|                           | MAJCOM  |  |
|                           | Medically treated with OCPs, progestin or NSAIDs  Medically treated with GnRH analog <sup>1</sup> Medically treated with OCPs, progestin or NSAIDs  Medically treated with GnRH analog <sup>1</sup> Medically treated with GnRH analog <sup>1</sup> |  |

<sup>1</sup> Gn-RH analogs are generally used for 2-3 months (rarely longer) in preparation of surgery and then discontinued. 2 No waiver required for ATC and MOD personnel unless unable to perform duties or treated with unapproved medications.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment. History should include degree of impairment from the symptomatic uterine fibroids, level of functioning before and after uterine fibroid treatment modalities, presence and/or resolution of anemia/fatigue, treatment modalities used, and treatment option considerations (e.g., future fertility desired).
- 2. Reports of any pertinent laboratory studies, imaging studies, copies of images (as indicated), including a current complete blood count.
- 3. Gynecology consultation report, including follow-up notes with examination findings after treatment.
- 4. Any specific diagnostic tests performed, before and after treatment (as indicated), including a histology report, if applicable.
- 5. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 6. Current physical examination findings.
- 7. Any other pertinent information.
- 8. The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

## B. Renewal Waiver Request:

- 1 Interval history since last aeromedical summary with emphasis on any symptoms compatible with the disorder.
- 2 Current complete blood count.
- 3 Consultation from gynecologist or treating physician.
- 4 The above list is not an absolute requirement list. If there is a valid reason for not including an important item in medical care, document why.

# **III. Aeromedical Concerns**

Symptomatic fibroids may cause significant distraction or impairment during flight due to dysmenorrhea, heavy menstrual bleeding, symptomatic anemia, and non-menstrual pain symptoms such as pressure, bloating, and urinary frequency and/or urgency. The medical treatment of fibroids can lead to side effects unacceptable for flying status. The use of hormone suppressive medications such as oral contraceptive pills, progesterone supplementation, or a progesterone containing intrauterine device are generally well tolerated and considered acceptable for flying duties. The use of other medications such as GnRH agonists/antagonists or aromatase inhibitors are often associated with significant and unpredictable symptoms. The symptoms associated with these can have an adverse effect on duty performance and symptoms may vary within and across patients. The GnRH medications are generally utilized on a temporary basis and typically in preparation for surgical treatment. All surgical treatments, including myomectomy, uterine artery embolization, and hysterectomy, due to the associated recovery period and possible complications, would be incompatible with flying duties until the individual is fully recovered and histology is confirmed as benign.

A review of AIMWTS through Feb 2019 revealed 14 aviators with an AMS containing the diagnosis of uterine fibroids; four were FC II (one disqualified) and ten were FC III (two disqualified). Of the three disqualifications, two cases had other disqualifying diagnoses and one case required optimization of treatment for symptom control.

| ICD-9 codes for | · Uterine Fibroids |
|-----------------|--------------------|
| 218             | Uterine leiomyoma  |

| ICD-10 codes for Uterine Fibroids |   |  |
|-----------------------------------|---|--|
| D25.9                             | Leiomyoma of uterus, unspecified            |  |
| N93                               | Other abnormal uterine and vaginal bleeding |  |

# IV. Suggested Readings

- 1. De La Cruz MD and Buchanan EM. Uterine Fibroids: Diagnosis and Treatment. Am Fam Physician, 2017; 95(2):100-107, https://www.aafp.org/afp/2017/0115/p100.html.
- 2. Mas A, Tarazona M, Carrasco JD, et al. Updated approaches for management of uterine fibroids. Intl J Women's Health, 2017; 9: 607.

- 3. Stewart EA. Uterine leiomyomas (fibroids): Epidemiology, clinical features, diagnosis, and natural history. UpToDate. Online version 28.0. Jun 2017.
- 4. Vilos G, Allaire C, Laberge P, Leyland N. The Management of Uterine Leiomyoma: SOGC Clinical Practice Guideline. J Obstet Gynaecol Can, 2015; 318:157-178.
- 5. Stewart EA. Overview of treatment of uterine leiomyomas (fibroids). UpToDate. Dec 2018. <a href="https://www.uptodate.com/contents/overview-of-treatment-of-uterine-leiomyomas-fibroids">https://www.uptodate.com/contents/overview-of-treatment-of-uterine-leiomyomas-fibroids</a>

## Uveitis (Mar 2020)

Reviewed: Lt Col Jonathan Ellis (Chief, ACS Ophthalmology), Lt Col Michael Parsons (Deputy Chief, ACS Ophthalmology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator) and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

New Ground Based Operator (GBO) Standards. MSD C38

## I. Waiver Consideration

Acute, chronic or recurrent inflammation of the uveal tract, except for healed traumatic iritis is disqualifying for flying classes I/IA, II, III, and SWA duties. For all initial flying classes, waivers will be considered if the uveitis was a single episode that occurred greater than one year ago, was nongranulomatous, unilateral, and did not result in recurrent episodes or ongoing visual symptoms or sequelae. Trained assets will be considered for a waiver. If the uveitis is secondary to a systemic disease, waiver consideration will also depend on the status of the causative systemic disease, see applicable waiver guides. While not specified in either AFI 48-123 or the MSD as disqualifying for ATC and GBO personnel, uveitis should be disqualifying if it is recurrent or chronic, leads to frequent absences from duty, or results in decrease or loss of vision.

**Table 1: Waiver potential for Uveitis** 

| Flying Class (FC)             | Waiver Potential   | Waiver Authority | ACS Review/Evaluation |
|-------------------------------|--------------------|------------------|-----------------------|
| I/IA or<br>II/III (untrained) | Maybe <sup>1</sup> | AETC             | Yes                   |
| II/III (trained)<br>SWA       | Yes                | MAJCOM           | Yes                   |
| ATC/GBO/OSF                   | N/A                | N/A              | N/A                   |

<sup>1.</sup> For all initial flying classes, waiver recommendation will be considered if the uveitis was a single episode that occurred greater than one year ago, nongranulomatous, unilateral, and did not result in recurrent episodes or ongoing visual symptoms or sequelae.

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines & recommendations.

# A. <u>Initial Waiver Request (Items 4-6 required for granulomatous, recurrent, or bilateral cases):</u>

- 1. History signs, symptoms, duration, treatment and must include pertinent review of system negatives.
- 2. Physical complete.
- 3. Ophthalmology consultation.
- 4. Chest x-ray to rule out sarcoidosis and tuberculosis.
- 5. Labs: Syphilis serology, Lyme titer, HLA-B27, erythrocyte sedimentation rate (ESR).
- 6. IPPD.

7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

## B. Waiver Renewal:

- 1. History signs, symptoms, duration, treatment and must include pertinent review of system negatives.
- 2. Physical complete.
- 3. Ophthalmology consultation.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to the waiver authority.

## **III. Aeromedical Concerns**

For the flight surgeon, uveitis of any etiology is of concern due to possible complications and sequelae. The acute condition can cause distracting pain. Floaters and blurred vision can impair performance and affect flight safety. Long-term sequelae include pupillary abnormalities, cataract, glaucoma, retinal scarring, retinal detachment, keratopathy, and loss of vision. The flight surgeon also needs to be concerned with possible underlying disease processes which may require aeromedical disposition as well.<sup>1</sup>

A review of the AIMWTS database in May 2015 revealed 137 cases of uveitis; 19 were disqualified. There were 0 FC I/IA cases, 72 FC II cases (5 disqualifications), 57 FC III cases (11 disqualifications), 6 ATC/GBC cases (2 disqualifications), and 2 MOD cases (1 disqualification). Of the 19 disqualified, all but 2 were secondary to the uveitis symptoms.

A review of the AIMWTS database in Jan 2019 revealed 109 cases of uveitis; 18 were disqualified. There was 1 FC I/IA cases (1 disqualified), 52 FC II cases (4 disqualified), 1 RPA pilot case, 47 FC III cases (10 disqualified), 6 ATC/GBC cases (2 disqualified), and 2 MOD cases (1 disqualified). Of the 18 disqualified, all but 2 were secondary to the uveitis symptoms.

| ICD-9 Codes for Uveitis |  |
|-------------------------|--|
| 364.3                   | Unspecified iridocyclitis                                  |
| 363.2                   | Unspecified forms of chorioretinitis and retinochoroiditis |
| 360.12                  | Panuveitis   |

| ICD-10 Codes for Uveitis |  |
|--------------------------|--|
| H20.9                    | Unspecified iridocyclitis              |
| H30.93                   | Unspecified chorioretinal inflammation |
| 1, 2, 3, 9               |  |
| H44.11                   | Panuveitis                             |
| 1, 2, 3, 9               |  |

## IV. Suggested Readings

1. Rayman R, Hastings J, Kruyer et al. Ophthalmology: Uveitis. Ch. 9 in *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., Castle Connolly Graduate Medical Publishing, Ltd; 2013: 280-83

# **WAIVER GUIDE**

Updated: May 2017

Supersedes Waiver Guide of Jan 2011

By: Lt Col Cindy Harris Graessle (RAM 2017) and Dr Dan Van Syoc

Reviewed by: Dr. Edwin Palileo and Lt Col Eddie Davenport (Chief Cardiologist ACS)

## **CONDITION:**

Valve Surgery - Replacement or Repair (May 2017)

# I. Waiver Consideration.

Cardiac valve replacement or repair by surgery or catheter-based technique is disqualifying for all classes of flying duties as well as retention in most cases. ACS review/evaluation is required for initial and renewal waiver considerations. The ACS will make recommendations based on the successfulness of the procedure/surgery and residual valve hemodynamics and cardiac function.

Table 1: Waiver potential for various valve replacements and repairs.

| Flying Class | Condition  | Waiver Potential | ACS               |
|--------------|--|------------------|-------------------|
| (FC)         |  | Waiver Authority | Evaluation/Review |
| Ī/IA         | Mitral valve, aortic valve and   | No               | No                |
|              | tricuspid valve surgery  | AETC             |                   |
|              |  |                  |                   |
|              | Pulmonic valvuloplasty   | Maybe            | Yes               |
|              |  | AFMRA            |                   |
| II/III       | Mitral valve prosthetic  | No               | No                |
|              | (mechanical or biological)   | AFMRA            |                   |
|              |  |                  |                   |
|              | Mitral valve annuloplasty or   | Maybe            | Yes               |
|              | repair   | AFMRA            |                   |
|              | Aortic valve (mechanical)  | No               | No                |
|              | Aortic varve (mechanical)  | AFMRA            | NO                |
|              |  | AIWIKA           |                   |
|              | Aortic valve (biological)  | Maybe            | Yes               |
|              | Tiorne varve (biological)  | AFMRA            | 103               |
|              |  |                  |                   |
|              | Other procedures or valves   | Maybe            | Yes               |
|              |  | AFMRA            |                   |
| III*         | Mitral valve prosthetic  | No               | No                |
| ATC/GBO/SWA* | (mechanical or biological)   | AFMRA            |                   |
|              |  |                  |                   |
|              | Mitral valve annuloplasty or   | Maybe            | Yes               |
|              | repair   | AFMRA            |                   |
|              |  | NT               | NT                |
|              | Aortic valve (mechanical)  | No               | No                |
|              |  | AFMRA            |                   |
|              | Aortic valve (biological)  | Maybe            | Yes               |
|              | Northe varve (biological)  | AFMRA            | 105               |
|              |  |                  |                   |
|              | Other procedures or valves   | Maybe            | Yes               |
|              | Paradament of the control of the con | AFMRA            |                   |

<sup>\*</sup>Waiver authority for all initial certification is AETC.

# II. Information Required for Waiver Submission.

Complete MEB prior to waiver submission. Prior to waiver submission for valve replacement or repair there is a minimum nonflying observation period of six months. After the six-month observation period, submit an aeromedical summary (AMS) with the following information:

- A. Complete history and physical exam to include description of symptoms before and after surgery, cardiovascular risks (family history, smoking status, lipids, and history of rheumatic disease), medications, and activity level.
- B. Copy of pre- and post-procedure local echocardiogram reports. For all FC II and RPA Pilots and for FC I and III individuals requiring ACS evaluation, send digital copy/CD copy of the echocardiographic images to the ACS. (Notes 1 and 2)
- C. Copy of the formal operation/procedure report and follow-up progress notes by the attending cardiovascular specialists.
- D. Copies of reports and tracings of any other cardiac tests performed locally for clinical assessment (e.g. electrocardiogram, treadmill, Holter monitor). For all FC II and RPA Pilots and for FC I and III individuals requiring ACS evaluation if reports or tracings not attached in AIMWTS then send to ACS. (Notes 1 and 2)
- E. Results of medical evaluation board MEB) (worldwide duty evaluation for ARC members).
- F. Additional local cardiac testing is not routinely required but may be requested in individual cases.

<u>Note 1</u>: Electronic submission of cardiac studies to the ECG library is preferred, please contact ECG library at USAFSAM.FECIECGLib@us.af.mil for access.

The address to send digital imaging/CD and reports not electronically submitted is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

For expediting case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

Note 2: State in AMS when studies were sent to ACS.

#### III. Overview.

Replacement or repair of a cardiac valve is a complicated aeromedical subject and disposition consideration. This is largely considered a surgical procedure; however, catheter-based techniques are presently being performed in certain cases. In the military aviator/aircrew population valve replacement or repair will usually be for severe regurgitation of the aortic or mitral valve. In the older aviator population with bicuspid aortic valve, significant aortic valve stenosis is an unusual possibility. Procedures for mitral stenosis and tricuspid valve disease are very rare. One occasional consideration in candidates for initial flying training may be balloon valvuloplasty of congenital pulmonary valve stenosis performed during childhood. Due to the broad spectrum of procedures, types of valve prostheses and other considerations, valve replacement/repair considered for waiver must be evaluated by the Aeromedical Consultation Service (ACS) (See Table 1). Information in this waiver guide will thus be very general.

## IV. Aeromedical Concerns.

Aeromedical concerns include thromboembolic events, anticoagulation and/or antiplatelet medications, infective endocarditis, dysrhythmias, residual or progressive post-procedure valvular regurgitation and/or stenosis, and short- and long-term durability of the procedure, especially prostheses. The etiology of the underlying valve disease is also a consideration as it may affect procedure outcomes (e.g. repair of severe mitral regurgitation (MR) due to myxomatous disease has a much better prognosis than severe MR due to rheumatic disease).

Prosthetic valves are of two basic types, mechanical (primarily metal) and biological (human and nonhuman tissue). Regardless of valve type, valve prostheses in the mitral position have higher thromboembolic rates than those in the aortic position and are thus unacceptable for military aviation. Mechanical valves have higher thromboembolic rates than biological valves and require chronic anticoagulation therapy, with associated risk of major hemorrhage. The combined risk is considered unacceptable for military aviation. Biological valve prostheses are of several tissue types and designs and do not require chronic warfarin therapy unless there is some other indication, such as chronic atrial fibrillation. These valves in the aortic position may be a consideration for waiver. Mitral valve repair and annuloplasty for severe MR due to a myxomatous valve (i.e. mitral valve prolapse) also may be favorably considered for waiver. Valve prostheses with residual regurgitation or other concerns regarding long-term durability will likely be restricted to low performance aircraft. Select architecturally intact valves with no residual regurgitation may be considered for unrestricted waiver on a case-by-case basis.

### V. References.

- 1. Bonow RO, Carabello B, DeLeon AC, et al. ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee on management of patients with valvular heart disease). J Am Coll Cardiol, 1998; 32: 1486-1588.
- 2. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Circulation, 2006; 114: e84-e231.
- 3. Bonow RO, Cheitlin MD, Crawford MH, and Douglas PS. 36th Bethesda conference: Eligibility recommendations for competitive athletes with cardiovascular abnormalities. Task force 3: Valvular heart disease. J Am Coll Cardiol, 2005; 45: 1334-40.
- 4. Cheitlin MD, Douglas PS, and Parmley WW. 26<sup>th</sup> Bethesda conference: Recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. Task force 2: Acquired valvular heart disease. J Am Coll Cardiol, 1994; 24: 874-80.
- 5. Holmes DR, Mack MJ, Kaul S, et al. 2012 ACCF/AATS/SCAI/STS Expert Consensus Document on Transcatheter Aortic Valve Replacement. J Thoracic Cardiovasc Surg, 2012; 144(3): e29-84

- 6. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med, 2016; 374(17): 1609-20.
- 7. Kruyer WB and Davenport ED. Cardiology. In *Rayman's Clinical Aviation Medicine*, 5<sup>th</sup> ed., Castle Connolly Graduate Medical Publishing, LTD, New York, 2013, 47-70.
- 8. Strader JR, Gray GW, and Kruyer WB. Clinical Aerospace Cardiovascular Medicine. In *Fundamentals of Aerospace Medicine*, 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2008; 333-38.
- 9. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (Version 2012). The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Euro J Cardio-Thoracic Surg, 2012; 42. S1-S44.
- 10. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol, 2014; 63(22): e57-e185.
- 11. Peltz M. Surgery for Valvular Heart Disease. Ch. 46 in *Cardiovascular Therapeutics: A Companion to Braunwald's Heart Disease*, 4<sup>th</sup> ed., Saunders, 2012.
- 12. Algarni KD, Suri RM, and Schaff H. Minimally invasive mitral valve surgery: Does it make a difference? Trends Cardiovasc Med, 2015; 25. 456-45.
- 13. O'Gara PT, Calhoon JH, Moon MR, and Tommaso CL. Transcatheter Therapies for Mitral Regurgitation. J Am Coll Cardiol, 2014; 63(8) 841-52.

## Venous Thromboembolism (VTE) (Dec 2019)

Authors/Reviewers: Capt Luke Menner, Dr. Christopher Keirns, and Maj Laura Bridge (ACS Internal Medicine); Dr. Dan Van Syoc (ACS Waiver Guide Coordinator)

**Significant Changes:** Waiver requirements, anticoagulation agents considered, and aeromedical concerns section updated.

## I. Waiver Consideration

Venous thromboembolism (VTE) is a term used to describe an episode of pulmonary embolism or deep vein thrombosis. Any history of pulmonary embolism is disqualifying for all flying classes, ATC, GBO, and special warfare personnel. It is also disqualifying for retention. Additionally, any history of deep vein thrombosis is disqualifying for FC I/IA/II/III, ATC and special warfare personnel. A single episode of deep vein thrombosis is not disqualifying for GBO. Recurrent episodes of deep vein thrombosis is disqualifying for all flying classes, GBO duties, ATC duties, and special warfare duties, as well as for retention. The use of extended (previously referred to as indefinite) anticoagulation is independently disqualifying for all flying and special duty operators as well as for retention.

Aeromedical waivers for venous thromboembolism may be considered after completion of at least three months of anticoagulation. Documentation must be provided to indicate whether the episode of VTE was provoked or unprovoked. Provoked VTE is defined by the presence of an underlying major transient risk factor (i.e., surgery, leg injury, flight > 8 hr, estrogen therapy, pregnancy). Individuals submitting waiver for unprovoked VTE or recurrent VTE require a complete hypercoaglulable evaluation and age-appropriate cancer screening performed prior to waiver submission. After a single episode of either provoked or unprovoked VTE, anticoagulation must be continued for a minimum of three months. Individuals in whom extended anticoagulation is deemed reasonable by the treating provider will require waiver and retention determination. Aeromedical waivers for trained pilots with VTE who require extended anticoagulation will be restricted to FC IIC, non-high performance, non-ejection seat, dual-control aircraft.

Historically, warfarin (Coumadin®) has been the anticoagulant of choice for individuals requiring extended anticoagulation since monitoring and reversal agents are readily available. However, the monitoring for warfarin can be operationally burdensome given the need for frequent laboratory testing and dose adjustments. Direct oral anticoagulants (DOACs) such as apixaban (Eliquis®), rivaroxaban (Xarelto®), dabigatran (Pradaxa®), and edoxaban (Savaysa®) do not require monitoring or dose adjustments. These short-acting medications have similar safety and efficacy to warfarin with some agents having lower rates of spontaneous cranial and gastrointestinal hemorrhaging. Additionally, reversal agents are available for apixaban, rivaroxaban, and dabigatran. Individuals treated with DOACs can be considered for an aeromedical waiver on a case-by-case basis.

Table 1: Waiver potential for VTE including DVT and PE

| Flying Class<br>(FC) | Condition <sup>1,2,3</sup>  | Wavier Potential<br>Waiver Authority | ACS Review or Evaluation |
|----------------------|---|--------------------------------------|--------------------------|
| I/IA                 | Provoked VTE, single episode, no longer requiring anticoagulation         | Yes<br>AETC                          | Yes                      |
|                      | Recurrent or unprovoked VTE   | No<br>AETC                           | No                       |
| II/III<br>ATC/SWA    | Provoked VTE, single episode <sup>4</sup>                                 | Yes<br>MAJCOM <sup>5</sup>           | Yes                      |
|                      | Recurrent VTE or unprovoked VTE <sup>4</sup>                              | Yes<br>MAJCOM <sup>5</sup>           | Yes                      |
| GBO                  | Deep vein thrombosis, single episode, no longer requiring anticoagulation | N/A                                  | N/A                      |
|                      | Pulmonary embolism, single episode  | Yes<br>MAJCOM <sup>5</sup>           | Yes                      |
|                      | Recurrent VTE or unprovoked VTE   | Yes<br>MAJCOM <sup>5</sup>           | Yes                      |

- 5. Waivers for VTE may be considered after completion of at least three months of anticoagulation.
- 6. Individuals with provoked VTE do not require a hypercoagulable workup. Individuals with unprovoked or recurrent VTE require a hypercoagulable workup to include testing for Factor V Leiden and prothrombin gene mutations, protein C, S, and antithrombin activity/levels, and antiphospholipid antibody testing.
- 7. All individuals requiring the use of extended anticoagulation require aeromedical waiver. Utilization of DOACs can be considered for waiver on a case-by-case basis.
- 8. Pilots requiring extended anticoagulation will be considered for a restricted waiver only (non-high performance, non-ejection seat, and dual-control aircraft). Similarly, special warfare personnel on extended anticoagulation will require restriction from jump duties.
- 9. AFMRA is the waiver authority for unapproved medications or restricted waivers.

# II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after the clinical disposition is complete and the service member is stable on all appropriate treatments, following the best current clinical guidelines and practice recommendations.

## A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment.
- 2. Consultation reports form all treating providers or specialists, which should include:
  - a. Documentation whether the VTE episode was provoked or unprovoked.
  - b. Hypercoagulable workup and age-appropriate cancer screening if VTE episode was unprovoked.
    - i. Should include testing for Factor V Leiden and prothrombin gene mutations, protein C, S, and antithrombin activity/levels, and antiphospholipid antibody testing
  - c. Current monitoring and treatment plan if individual requires extended anticoagulation.
  - d. Documentation of any associated complications such as post-thrombotic syndrome or chronic thromboembolic pulmonary hypertension (CTEPH).
- 3. Reports of any other pertinent laboratory studies or imaging studies obtained.
  - a. Current d-dimer.
  - b. Current CBC if on anticoagulation. If warfarin is the anticoagulant being utilized, INR values from the preceding three months should be provided.
- 4. Any specific diagnostic tests performed, before and after treatment (as indicated).
  - a. Individuals diagnosed with a pulmonary embolism require a full pulmonary function testing and repeat CT pulmonary angiogram (CTPA) after completion of three months of therapy and prior to waiver submission.
- 5. Current physical examination findings.
- 6. FL4 with RTD and ALC status, if applicable.
- 7. Any other pertinent information.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

## B. Renewal Waiver Request:

- 1 Updated AMS with interval history.
- 2 Consultation reports from treating specialist if applicable including current monitoring and treatment plan if individual requires extended anticoagulation.
- 3 Any interval imaging obtained pertaining to the episode of VTE and updated CBC if on anticoagulation.
- 4 Current physical examination findings.
- 5 Any other pertinent information.
- 6 If the local base cannot provide any of the above listed information, they should document why, explaining the reason to the waiver authority.

### III. Aeromedical Concerns

Venous thromboembolism (VTE) presenting as a symptomatic deep vein thrombosis (DVT) or pulmonary embolism (PE) can potentially result in distracting or incapacitating symptoms. Acute DVT may cause symptoms such as swelling and distracting pain. Rarely, significant swelling may lead to neurovascular compromise of the affected limb. Post-thrombotic syndrome is a potential sequelae that can result in recurrent swelling and distracting symptoms. The development of subsegmental pulmonary embolisms may lead to dyspnea and chest pain. Submassive or massive pulmonary embolisms may lead to cardiovascular collapse. The most aeromedical concerning

chronic sequelae from pulmonary embolisms is the development of chronic thromboembolic pulmonary hypertension (CTEPH), which would increase the risk of developing hypoxia at altitude, right-sided heart failure, and cardiac arrhythmias.

After completing treatment for an acute episode of VTE, an additional aeromedical concern is the development of a recurrent event. The highest risk of recurrence is within the first year, and individuals with unprovoked VTE are at a higher risk of recurrent events then an individual with a provoked VTE. VTE provoked by surgery is estimated to have a 3% risk of recurrence at 5 years. VTE provoked by a nonsurgical major transient risk factor (i.e., leg injury, flight of >8hrs, estrogen therapy, or pregnancy) has a 15% risk of recurrence at 5 years. Unprovoked VTE not involving a major transient risk factor has a 30% risk of recurrence at 5 years. Thus, individuals with unprovoked VTE should undergo a hypercoagulable workup and age appropriate cancer screening to evaluate for any underlying condition that predisposes to recurrent events. This data was derived from the CEHST guidelines for antithrombotic therapy for VTE disease.

Treatment options to reduce the risk of recurrent episodes of VTE have greatly expanded over the past decade. There are no current anticoagulants on any career-field approved medication lists. However, warfarin (Coumadin®) has been waivered on a case-by-case basis for many years and it historically was the preferred agent due to the ability to monitor adherence and the availability of a reversal agent. As noted above, laboratory monitoring and the need for dose adjustments can become operationally burdensome with warfarin utilization. Direct oral anticoagulants (DOACs) such as apixaban (Eliquis ®), rivaroxaban (Xarelto®), dabigatran (Pradaxa®), and edoxaban (Savaysa®) do not require monitoring or dose adjustments. These short-acting medications have similar safety and efficacy compared to warfarin with some agents having lower rates of spontaneous cranial and gastrointestinal hemorrhaging. Additionally, reversal agents are available for apixaban, rivaroxaban, and dabigatran. Individuals treated with DOACs have recently been considered for an aeromedical waiver on a case-by-case basis. The greatest aeromedical concern of current anticoagulation use is the aviation environment is the development of spontaneous cranial, spontaneous gastrointestinal, or traumatic hemorrhaging. The risk of developing spontaneous bleeding is low in young individuals without any significant comorbidities. There are several validated tools to estimate the risk of developing spontaneous bleeding such as the HAS-BLED tool. Although this specific model was designed looking at individuals with atrial fibrillation treated with anticoagulation to prevent embolic strokes, this tool can be used to assess if the risk of spontaneous bleeding with use of extended anticoagulation outweighs the risk of recurrent VTE. Traumatic hemorrhaging in an austere environment is a significant aeromedical risk. Some career fields such as special warfare airmen have duty requirements that may not be compatible with the use of extended anticoagulation.

Review of the AIMWTS database from Jan 2015 through Nov 2019 revealed 50 individuals with an AMS containing the diagnosis of VTE. Seven individuals (14%) were disqualified. A breakdown of the cases was follows: 5 FC I/IA cases (1 disqualified), 25 FC II cases (4 disqualified), 13 FC III cases (2 disqualified), 4 ATC/GBC cases (0 disqualified), 0 MOD cases, and 3 RPA Pilot cases (0 disqualified).

| ICD-9 codes for Venous Thromboembolism (VTE) |                        |
|--|------------------------|
| 453.89                                       | Deep venous thrombosis |
| 415.1  | Pulmonary embolism     |

| ICD-10 codes for Venous Thromboembolism (VTE) |                        |
|---|------------------------|
| I82.9   | Deep venous thrombosis |
| I26.9   | Pulmonary embolism     |

# **IV. Suggested Readings**

- 1. Kearon C, Akl EA, Ornalas, J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. CHEST: 2016; 149(2):315-352. https://www.ncbi.nlm.nih.gov/pubmed/26867832
- 2. Tristschler T, Kraaijpoel N, Le Gal G, et al. Venous Thromboembolism: Advances in Diagnosis and Treatment. JAMA. 2018; 320(15):1583-1594.

# Ventricular Tachycarhia (Dec 2019)

Reviewed: Capt Mitchell Radigan (RAM 20), Lt Col Eddie Davenport (ACS Cardiology), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator, and Lt Col David Gregory (AFMRA Physical Standards Development Chief)

# **Significant Changes:**

Updated content and format

## I. Waiver Consideration

Ventricular tachycardia (VT) is the most malignant of arrhythmias which can degenerate into ventricular fibrillation and sudden death; therefore immediate DNIF is required in all documented VT until a complete investigation can be completed. VT may be symptom of structural heart disease, ischemia, infarction, cardiomyopathy, or channelopathy. A history of symptomatic or asymptomatic ventricular tachycardia is disqualifying for all classes of flying duties. VT is defined as 3 or more consecutive complexes originating in the ventricles at a rate of >100bpm and can be sustained (>30 sec or requiring termination due to hemodynamic compromise) or non-sustained (terminating spontaneously) and monomorphic (stable morphology) or polymorphic (changing or multiform QRS from beat to beat). VT is considered significant and disqualifying if associated with hemodynamic symptoms, an underlying cardiac disorder, is longer than 11 beats, or when there are more than 4 episodes of VT in a single exercise stress test or during a 24 hour Holter monitor. VT that can be treated via aeromedically approved medications or ablation is waiverable for all flying classes in asymptomatic aircrew with a structurally normal heart. Given the complexity of cases, ACS review is recommended in all VT waivers. FC I, FC II and FC III waivers for VT require ACS evaluation/review.

Table 1 summarizes the current approved aeromedical policy.

Table 1: Waiver potential for Ventricular Tachycardia

| Flying Class  | r potential for Ventricular Tacnycardia<br>     | Waiver Authority | ACS Review/   |
|---------------|---|------------------|---------------|
| (FC)          | Disease/Condition                               | Waiver Potential | Evaluation    |
| I/IA          | Nonsustained idiopathic VT (max                 | Maybe            | Yes           |
| Untrained II, | duration <11 beats, <4 episodes per             | AETC             |               |
| RPA pilot,    | study)  |                  |               |
| and III       |   |                  |               |
|               | Nonsustained idiopathic VT (max                 | Maybe            | Yes           |
|               | duration >11 beats, >4 episodes per             | AETC             |               |
|               | study) or sustained VT after ablation           |                  |               |
|               | Nonsustained VT with underlying                 | No               | No            |
|               | cardiac disorder <sup>1</sup>                   | AETC             |               |
|               | Sustained VT or any duration VT with            | No               | No            |
|               | associated hemodynamic symptoms                 | AETC             |               |
|               | not treatable with ablation.                    |                  |               |
| II/III        | Nonsustained idiopathic VT (max                 | Yes              | Yes           |
|               | duration $\leq 11$ beats, $\leq 4$ episodes per | MAJCOM           |               |
|               | study)  |                  |               |
|               | Nonsustained idiopathic VT (max                 | Maybe            | Yes           |
|               | duration >11 beats, >4 episodes per             | MAJCOM           |               |
|               | study) or sustained VT after ablation           |                  |               |
|               | Nonsustained VT with underlying                 | Maybe            | Yes           |
|               | cardiac disorder <sup>1</sup>                   | MAJCOM           |               |
|               | Sustained VT or any duration VT with            | No               | No            |
|               | associated hemodynamic symptoms                 | MAJCOM*          |               |
|               | not treatable with ablation.                    |                  |               |
| ATC           | Any sustained VT with or without                | Yes              | Yes           |
| GBO           | medical treatment or ablation                   | MAJCOM           |               |
| SWA           |   | **               | A 1           |
|               | Any Nonsustained VT                             | Yes              | At the        |
|               |   |                  | discretion of |
|               |   |                  | the waiver    |
|               |   |                  | authority     |

<sup>1.</sup> Cardiac disorders that are unlikely to be waived include moderate and significant coronary artery disease, hypertrophic or dilated cardiomyopathy, and electrical or ion-channel abnormalities (unless potentially curable with ablation).

# **II. Information Required for Waiver Submittal**

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed and all appropriate treatments have been initiated using best current clinical guidelines and recommendations.

# A. Initial Waiver Request:

- 1. Summary of presentation, course, and treatment, including:
  - a. Detailed description of VT and of symptoms before and after the acute episode
  - b. Medications, lab values
  - c. Activity level
  - d. CAD risk factors (positive and negative)
  - e. Electrophysiology Reports if performed

There is no minimum required nonflying observation period for waiver consideration for nonsustained VT.

- 2. Reports of any pertinent laboratory studies and actual ECG tracings and images (as indicated). Include diagnostic tests and procedures performed to include EKG, ambulatory ECG monitor, treadmill test, echocardiogram, cardiac MRI/CT, EP studies etc. No additional studies are required, unless specifically requested on a case by case basis, prior to ACS evaluation. If however, the treating physician deems it clinically necessary to perform additional studies, it is required that all studies be forwarded to the ACS for review.
- 3. Any consultation reports, including follow-up notes with examination findings after disease resolution.
- 4. Documentation of return to full physical activity, including specific comments regarding any activity limitations.
- 5. Current physical examination findings.
- 6. FL4 with RTD and ALC status, if member did not meet retention status
- 7. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### B. Renewal Waiver Request:

- 1 Summary of interim course and treatment including:
  - a. Change in symptoms
  - b. Medications
  - c. Activity level
  - d. CAD risk factors (positive and negative).
- 2 Reports of any pertinent laboratory studies or cardiac imaging studies that have been done since initial waiver. No additional studies are required, unless specifically requested on a case-by-case basis, prior to ACS evaluation. If however, the treating physician deems it clinically necessary to perform additional studies, it is required that all studies be forwarded to the ACS for review.
- 3 Any follow-up or new consultation reports.
- 4 Documentation of degree of physical activity, including specific comments regarding any activity limitations.
- 5 Current physical examination findings.

6 If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

<u>Note 1</u>: All studies should be submitted electronically to the EKG Library. If this is not possible, items can be mailed via FedEx. If mailed, include patient's name, SSN and POC at base:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

Note 2: State in AMS when studies were sent to the ACS.

#### **III. Aeromedical Concerns**

Ventricular tachycardia is second only to ventricular fibrillation as the most common cause of sudden cardiac death. In rare instances, VT can be associated with treatable electrolyte abnormalities and/or electrical re-entry which can be ablated and therefore waiverable. However, more often VT is the result of structural heart disease, ischemia, infarction, cardiomyopathy or channelopathy that in not compatible with ongoing flight duties given risk of hemodynamic symptoms that may render an individual incapable of remaining in control of an aircraft or supporting the flying mission. Though sudden cardiac death related to sustained VT would be an obvious and dramatic explanation for such an event, a less dramatic near syncopal episode is also likely to result in sudden incapacitation or interference with duty performance. Permanent disqualification for aircrew is recommended for VT, which is sustained or symptomatic, if antiarrhythmics are necessary for control, with AICD implantation, if associated with underlying myocardial disease, or when ablation is done for failed medical therapy in prior infarct/scar related VT.

When there is no underlying cardiac disease or other obvious etiology, the arrhythmia is termed *idiopathic VT*. Cardiac literature does support a benign prognosis for infrequent episodes of short-duration asymptomatic VT in structurally normal hearts. In USAF aviators with asymptomatic idiopathic non-sustained VT, the annual event rate for sudden cardiac death, syncope, presyncope, or sustained VT was less than 0.5% per year during a mean follow-up of approximately 10 years with the majority having VT runs of only three beats' duration and only one VT episode per 24-hour ambulatory ECG recording. Only 10% had more than four episodes of non-sustained VT per 24-hour ambulatory recording and only 3% had VT episodes longer than ten beats duration. International consensus is that asymptomatic VT with a duration of 11 beats or less and no more than 4 runs in a 24 hour period is acceptable for return to flight duties in otherwise structurally normal hearts. Idiopathic VT that responds well to antiarrhythmic therapy is limited by the side effect profile, pro-arrhythmic, and hemodynamic effects of antiarrhythmics. The only antiarrhythmic approved in aircrew is beta-blocker use in non-high performance airframes.

Review of AIMWTS waiver submissions for ventricular tachycardia in Nov 2019 for the previous 5 years showed 33 waivers submitted. Breakdown of the cases was as follows: 1 FC I/IA case (0 disqualified), 16 FC II cases (0 disqualified). 12 FC III cases (2 disqualified), 3 ATC/GBC cases (0 disqualified), and 1 SWA case (0 disqualified). There were a total of 2 submissions that resulted in

a disqualification. These were complex cases. One was associated with significant heart defects and the other had multiple comorbidities.

| ICD-9 codes for Disease/Condition |                                    |
|-----------------------------------|------------------------------------|
| 427.1                             | Paroxysmal ventricular tachycardia |

| ICD-10 codes for Disease/Condition |                         |
|------------------------------------|-------------------------|
| I47.2                              | Ventricular tachycardia |

# IV. Suggested Readings

- 1. Kruyer WB and Davenport ED. Cardiology. In: Rayman 's *Clinical Aviation Medicine*, 5<sup>th</sup> ed. New York: Castle Connolly Graduate Medical Publishing, LTD, 2013; 81-7.
- 2. Guettler N, Bron D, Manen O, et al. Management of cardiac conduction abnormalities and arrhythmia in aircrew. Assessing aeromedical risk: a three-dimensional risk matrix approach. Heart 2019;105:s38–s49
- 3. Sharma, S, Drezner J, Baggish A, Papadakis M et al. International Recommendations for Electrocardiographic Interpretation in Athletes. J Am Coll Cardiol 2017;69:1057–75
- 4. Marine, JE. Nonsustained ventricular tachycardia in the normal heart. Cardiac Electrophysiology Clinics, 2016; 8(3): 525-543.
- 5. Gardner RA, Kruyer WB, Pickard JS, and Celio PV. Nonsustained Ventricular Tachycardia in 193 U.S. Military Aviators: Long-Term Follow-Up. Aviat Space Environ Med, 2000; 71(8): 783-90.
- 6. Ramirez, A, Alvarado, RL, Lopez, FM, et al. A comparison of nonsustained ventricular tachycardia in military aviators with and without underlying structural heart disease. Aviat Space Environ Med, 2007; 78(3): 311.
- 7. Walker J, Calkins H and Nazarian S. Evaluation of Cardiac Arrhythmias Among Athletes. Am J Med, 2010; 123 1075-81.
- 8. Hoffmayer KS and Gerstenfeld EP. Diagnosis and Management of Idiopathic Ventricular Tachycardia. Curr Probl Cardiol, 2013; 28: 131-58.
- 9. Olgin J and Zipes DP. Specific Arrhythmias: Diagnosis and Treatment. Ch. 39 in *Bonow: Braunwald's Heart Disease A Textbook of Cardiovascular Medicine*, 9<sup>th</sup> ed., 2011, Saunders.
- 11. Huikuri HV, Castellanos A, and Myerburg RJ. Sudden Death Due to Cardiac Arrhythmias. N Engl J Med, 2001; 345(20): 1473-82.

# **Vertiginous Disorders, Peripheral (Mar 2020)**

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Division Deputy Chief), and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated Table 1 and References

### I. Waiver Consideration

Air Force aviators with vertigo of any etiology are disqualified for all flying classes, and need to be carefully evaluated before waiver consideration. For waiver consideration, all symptoms must have resolved, with sufficiently normal remaining vestibular function that would not cause clinical disability. Vestibular neuronitis is the only major form of peripheral vertigo to have a minimal risk of recurrence, and is the only form of peripheral vertigo for which FC I and unrestricted FC II waivers may be recommended. The likelihood of recurrence of benign paroxysmal positional vertigo is unacceptably high and precludes aeromedical waiver consideration except in cases with prolonged remission. Ménière's disease has unpredictable and recurrent symptoms with potential for sudden incapacitation, which also precludes aeromedical waiver consideration except in cases with prolonged remission. Superior semicircular canal dehiscence cases, if confirmed by temporal bone CT imaging and resolved with definitive treatment, may then be considered for aeromedical waiver. Aviators with unexplained vertigo, dizziness or disequilibrium symptoms without a definitive diagnosis are generally not recommended for aeromedical waiver due to inability to assess or predict future recurrence risk.

Table 1: Waiver potential for peripheral vertiginous disorders

| Flying Class (FC) | Waiver Potential | Waiver Authority | ACS Review or Evaluation          |
|-------------------|------------------|------------------|-----------------------------------|
| FC I/IA           | Yes <sup>1</sup> | AETC             | No                                |
| FC II/III/SWA     | Yes <sup>2</sup> | MAJCOM/AFMRA     | Yes                               |
| ATC/GBO           | Yes              | MAJCOM           | At discretion of waiver authority |

<sup>1.</sup> IFC I/IA waiver recommended only for cases of resolved vestibular neuronitis

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

### A. Initial Waiver Request:

1. Careful history describing: frequency, duration, severity and character of vertiginous attacks; type of maneuvers that provoke symptoms; presence or absence of associated symptoms such as hearing loss, aural fullness, tinnitus, headaches, or focal neurologic symptoms. Also note any past history of syphilis, mumps or other serious infections, inflammation of the eye, autoimmune disorder or allergy, and ear surgery.

<sup>2.</sup> Multi-place aircraft waiver generally recommended in cases of Ménière's disease with prolonged remission.

- 2. Otolaryngology consultation notes. For complex or undiagnosed cases, strongly consider obtaining formal Neuro-Otology consultation through SAMMC or an academic medical center.
- 3. Audiogram results, to include speech discrimination, tympanometry and acoustic reflexes.
- 4. Vestibular function testing results, which may include electronystagmography (ENG, VNG and calorics), vestibular evoked myogenic potentials (VEMP), computerized dynamic posturography (CDP), and rotary chair testing.
- 5. Laboratory testing results, which may include CBC, ESR, TFTs, lipids, glucose and syphilis serology.
- 6. Pre/post-contrast MRI of the brain and internal auditory canal (IAC) to rule out retrocochlear pathology such as cerebello-pontine angle (CPA) tumors, multiple sclerosis, anatomical variants, etc. Send report and images for review and reference. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without requiring administrative privileges.
- 7. Current physical, ENT and neurologic examination findings. Include assessment for nystagmus, balance, and results of Dix-Hallpike testing.
- 8. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

## B. Renewal Waiver Request:

- 1. Interval history and level of symptom resolution.
- 2. Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without requiring administrative privileges.
- 3. Current physical, ENT and neurologic examination findings. Include assessment for nystagmus, balance, and results of Dix-Hallpike testing.
- 4. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

#### III. Aeromedical Concerns

Aeromedical concerns include the effects of any residual symptoms on operational safety and mission effectiveness, future risk of new symptom development, and future risk of recurrence. The threat posed by ongoing vertigo in the flying environment is self-evident. Since all vertigo is potentially incapacitating (albeit to varying degrees), whether a syndrome is likely to recur or not following apparent resolution of symptoms is the key to whether an aeromedical waiver may be considered. Vestibular neuronitis is the only major form of peripheral vertigo to have a minimal risk of recurrence. The likelihood of recurrence of Benign Paroxysmal Positional Vertigo (15-18% in the first year, with a cumulative recurrence rate of 50% in five years) precludes aeromedical waiver consideration unless prolonged remission occurs. Even in cases with prolonged remission, categorical multi-place aircraft waiver is recommended. Ménière's disease has unpredictable and recurrent symptoms with potential for sudden incapacitation, and few reliable, aeromedically-compatible treatment options. Aeromedical waiver would therefore be recommended only under exceptional circumstances, such as cases with prolonged remission. Superior semicircular canal dehiscence produces symptoms evoked by loud noises or pressure-changing maneuvers such as

coughing, straining or sneezing. If confirmed by temporal bone CT imaging, definitive treatment is possible by surgical resurfacing or plugging the superior semicircular canal. Migrainous vertigo may respond to migraine medications and be potentially waiverable. Cases of unexplained vertigo, dizziness or disequilibrium with no definitive diagnosis are generally not recommended for aeromedical waiver due to inability to accurately assess future recurrence risk.

AIMWITS search in Jan 2019 revealed a total of 250 aviators with the diagnosis of vertigo. A total of 96 were disqualified. Breakdown of the cases revealed: 9 FC I/IA cases (5 disqualified), 135 FC II cases (36 disqualified), 5 RPA pilot cases (2 disqualified), 71 FC III cases (38 disqualified), 25 ATC/GBC cases (12 disqualified), and 5 MOD cases (3 disqualified). The diagnosis of vertigo was a factor is all 96 disqualified cases.

| ICD-9 codes for peripheral vertiginous disorders |  |  |
|--|--|--|
| 386.0  | Ménière's Disease                      |  |
| 386.10   | Peripheral vertigo, unspecified        |  |
| 386.11   | Benign paroxysmal positional vertigo   |  |
| 386.12   | Vestibular neuronitis                  |  |
| 386.19   | Other peripheral vertigo               |  |
| 386.30   | Labyrinthitis                          |  |
| 386.8  | Superior Semicircular Canal Dehiscence |  |

| ICD-10 cod | es for peripheral vertiginous disorders |
|------------|---|
| H81.4      | Vertigo of central origin               |
| 1, 2, 3, 9 |   |
| H81.0      | Ménière's Disease                       |
| 1, 2, 3, 9 |   |
| H81.39     | Other peripheral vertigo                |
| 1, 2, 3, 9 |   |
| H81.13     | Benign paroxysmal positional vertigo    |
| 1, 2, 3, 9 |   |
| H81.2      | Vestibular neuronitis                   |
| 1, 2, 3, 9 |   |
| H81.31     | Aural vertigo, unspecified ear          |
| 1, 2, 3, 9 |   |
| H83.0      | Labyrinthitis                           |
| 1, 2, 3, 9 |   |
| H83.1      | Labyrinthine fistula                    |
| 1, 2, 3, 9 |   |
| H83.8X9    | Superior Semicircular Canal Dehiscence  |

# IV. Suggested Readings

- 1. Moskowitz HS and Dinces EA. Ménière's disease. UpToDate, Oct 2, 2019.
- 2. Robertson CE and Eggers SDZ. Vestibular migraine. UpToDate, Dec 12, 2018.

- 3. Fife TD. Dizziness in the outpatient care setting. Continuum (Minneap Minn) 2017; 23(2):359-395.
- 4. Furman JM. Causes of vertigo. UpToDate, Aug 24, 2018.
- 5. Barton JSS. Benign paroxysmal positional vertigo. UpToDate, Dec 17, 2018.
- 6. Furman JM and Barton JSS. Evaluation of the patient with vertigo. UpToDate, Feb 11, 2020.
- 7. Ropper AH, Samuels MA, Klein JP (Ed). Dizziness, deafness and disorders of equilibrium. *Adams and Victor's Principles of Neurology*, Tenth Edition, McGraw-Hill Education, 2014:290-316.
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- 9. Furman JM. Vestibular neuronitis and labyrinthitis. UpToDate, Jul 18, 2018.
- 10. Packer MD and Welling DB. Surgery of the Endolymphatic Sac. Ch. 34 in *Otologic Surgery*, 3<sup>rd</sup> edition. Elsevier Inc., Editors Derald Brackmann, Clough Shelton, Moises Arriaga, 2010.

# Vestibular Schwannoma (Acoustic Neuroma) (Mar 2020)

Reviewed: Dr. Roger Hesselbrock (ACS Neurologist), Dr. Dan Van Syoc (ACS Waiver Guide Coordinator), Lt Col Wesley Abadie (AF/SG Otolaryngology Consultant) and Lt Col David Gregory (AFMSA Physical Standards Development Chief)

# **Significant Changes:**

Updated Table 1 and References

## I. Waiver Consideration

Vestibular Schwannoma (VS) is addressed in the USAF Medical Standards Directory (MSD) as "acoustic neuroma" and as "intracranial, meningeal, or other neurologic benign or malignant neoplasm". Newly-diagnosed VS is disqualifying for FC I/IA, II (as well as initial FC II), III, and for retention. VS are benign, slow-growing neoplasms that produce clinical symptoms primarily from local compression. Symptoms are often gradually progressive but may be insidious, with the potential for sudden development of symptoms. For aeromedical waiver consideration, the tumor must be unilateral, and there must be complete resolution of symptoms post-treatment. For aviators in high performance aircraft, in-flight or centrifuge testing should be strongly considered, to validate vestibular reserve is adequate to maintain awareness during maneuvers without sequelae. Any residual cranial nerve deficits should allow adequate communication, full ocular movements without tracking deficits or strabismus, and permit acceptable protective mask sealing. Confirmation of tumor pathology is needed with surgical cases, and surveillance MRI scanning is needed in cases treated non-invasively, to ensure stability and monitor for any growth. A history of previously-treated VS is not disqualifying for ATC, SWA and GBO personnel (except for initial RPA operators).

Table 1: Waiver potential for vestibular schwannoma

| Flying Class (FC) | Waiver Potential   | Waiver Authority | ACS Review or Evaluation |
|-------------------|--------------------|------------------|--------------------------|
| FC I/IA           | No                 | AETC             | No                       |
| FC II/III         | Yes <sup>1</sup>   | MAJCOM           | Yes                      |
| GBO/ATC/SWA       | Yes <sup>1,2</sup> | MAJCOM           | Yes <sup>2</sup>         |

<sup>1.</sup> If treated surgically or with radiation, minimum 6 month observation following definitive treatment, with no aeromedically-significant symptoms

## II. Information Required for Waiver Submittal

The aeromedical summary (AMS) should only be submitted after diagnostic evaluation has been completed, all appropriate treatments have been initiated using best current clinical guidelines and recommendations, and the member is clinically stable.

## A. Initial Waiver Request:

- 1. History symptoms, hearing exams prior to treatment, treatment course, post-surgical vertigo symptoms, and confirmed resolution of vestibular symptoms.
- 2. Current Otolaryngology evaluation, ocular and neurologic examination findings.
- 3. Current audiogram results.

<sup>2.</sup> History of VS is not disqualifying for GBO (except initial RPA operators), SWA, and ATC personnel.

- 4. Vestibular function testing results, which may include electronystagmography (ENG, VNG and calorics), and computerized dynamic posturography (CDP) testing.
- 5. Reports of consultations, surgical procedures, pathology reports or radiation therapy treatment reports, as applicable. For complex or undiagnosed cases, strongly consider obtaining formal Neuro-Otology consultation through SAMMC, WRNMMC, or an academic medical center.
- 6. Reports and images from any imaging studies, pre- and post-treatment. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 7. Tumor board report as applicable.
- 8. Medical Evaluation Board results as applicable.
- 9. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

# B. Renewal Waiver Request:

- 1. Interval history and level of symptom resolution.
- 2. Copies of any applicable interim specialty reports, labs, imaging reports and images. If images are sent to ACS on CD, please ensure that the images can be viewed on a standard AF desktop system without needing administrative privileges.
- 3. Copy of current audiogram.
- 4. Current physical, otolaryngology and neurologic examination findings.
- 5. If the local base cannot provide any of the above listed information, they should document why, explaining reasoning to waiver authority.

### **III. Aeromedical Concerns**

Aeromedical concerns include the effects of any residual symptoms on operational safety and mission effectiveness, future risk of new symptom development, and future risk of recurrence. Symptoms associated with VS are typically attributed to compression of associated cranial nerves (VIII, VII, IV, IX, X), cerebellar compression, and ultimately restricted CSF flow and hydrocephalus or brainstem compression. Tumors are unilateral in over 90 percent of cases. Bilateral VS is pathognomonic of the autosomal dominant genetic disorder neurofibromatosis type 2 (NF-2). The acoustic portion of VIII is involved in almost all cases, with the vestibular, trigeminal and facial nerves involved less frequently. Any aviator with asymmetric hearing loss, especially if progressive, should be screened for VS, as many VS are discovered after observing changes in annual audiograms. Cochlear and vestibular symptoms are of obvious importance to the aviator. Hearing loss and tinnitus can adversely impact communications, while vertigo and disequilibrium can adversely affect the ability to safely control an aircraft. Observation is a reasonable option with small, intracanicular tumors. Surveillance by follow up MRI scanning at 6 months, and then annually is reasonable. However, due to the wide range of progressive and potentially abrupt symptomatology, conservative observational management may be incompatible with the safe performance of aviation-related duties in some cases. In surgically treated patients, complete tumor removal can be accomplished in most cases, with minimal recurrence risk. Worsening of vestibular symptoms is commonly seen following surgical removal, but typically resolves by neurologic compensation with time and rehabilitation. The risk of cerebrospinal fluid leak is variable depending on type of surgery, but is between 6-11% and may require revision surgery or lumbar drainage to resolve. As opposed to total removal of the tumor with conventional

surgery, stereotactic radiation treatment is intended to stop tumor growth. In such cases, post-radiotherapy surveillance is necessary to ensure continued control over time. Delayed and slow responses are typical with stereotactic radiosurgery. Some tumors fail to respond to radiation and continue to grow, or are controlled initially, but resume growth over time. All post-operative or post-radiation vestibular symptoms require sustained documentation of compensation over time (e.g. radiation effects may manifest 18-24 months after irradiation) prior to waiver consideration, and any hearing loss needs to be stabilized and well documented by competent audiology services. An in-flight hearing evaluation may be required prior to clearing an aviator for flying duties. A good online resource is the Acoustic Neuroma Association site at <a href="www.anausa.org">www.anausa.org</a> which provides up-to-date information for patients and clinicians regarding this condition.

A review of AIMWTS through Mar 2019 revealed 35 cases. Breakdown of these cases revealed: 1 FC I/IA cases, 21 FC II cases, 1 RPA pilot case, and 12 FC III cases (4 disqualified)

| ICD-9 Codes for Vestibular Schwannoma |                                   |
|---------------------------------------|-----------------------------------|
| 225.1                                 | Benign Neoplasm of Cranial Nerves |
| 388.5                                 | Disorders of Acoustic Nerve       |

| ICD-10 Codes for Vestibular Schwannoma |                                   |  |
|--|-----------------------------------|--|
| D33.3                                  | Benign Neoplasm of Cranial Nerves |  |
| 1, 2, 3, 9                             |                                   |  |
| H93.3X                                 | Disorders of Acoustic Nerve       |  |
| 1, 2, 3, 9                             |                                   |  |

## **IV. Suggested Readings**

- 1. Evans DG. Neurofibromatosis type 2. UpToDate, Feb 14, 2020.
- 2. Park JK, Vernick DM, Ramakrishna N. Vestibular schwannoma (acoustic neuroma). UpToDate, Mar 25, 2019.
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- 4. Carlson ML et al. The changing landscape of vestibular schwannoma management in the United States a shift toward conservatism. Otolaryngol Head Neck Surg 2015; 153(3):440-446.
- 5. Ropper AH, Samuels MA, Klein JP (Ed). Dizziness, deafness and disorders of equilibrium. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:290-316.
- 6. Ropper AH, Samuels MA, Klein JP (Ed). Intracranial neoplasms and paraneoplastic disorders. *Adams and Victor's Principles of Neurology, Tenth Edition, McGraw-Hill Education*, 2014:639-696.
- 7. Casto KL and Choo TH. In-flight speech intelligibility evaluation of a service member with sensorineural hearing loss: a case report. Military Med 2012; 17 (9):1114-1116.

- 8. Kondziolka D, Mousavi SH, Kano H, et al. The newly diagnosed vestibular schwannoma: radiosurgery, resection, or observation? Neurosurg Focus 2012; 33(3):E8.
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#### WAIVER GUIDE

Updated: Jan 2018

Supersedes Waiver Guide of May 2013

By: Major Daniel R. Hatcher (RAM 2018) and Dr Dan Van Syoc

Reviewed by: Lt Col Eddie Davenport (ACS Chief Cardiologist) and AFMSA staff

# **CONDITION:**

Wolff-Parkinson-White (WPW) and other Pre-Excitation Syndromes (Jan 2018)

## I. Waiver Consideration.

Per MSD H14, WPW pattern is disqualifying for all classes of flying duties in the US Air Force.

Table 1: Waiver potential for WPW and related syndromes

| Flying Class (FC) | Waiver Potential<br>Waiver Authority | ACS Evaluation/Review |
|-------------------|--------------------------------------|-----------------------|
| I/IA              | Yes*                                 | Yes                   |
|                   | AETC                                 |                       |
| II/III            | Yes*                                 | Yes                   |
|                   | MAJCOM                               |                       |
| ATC/GBO/SWA       | Yes*                                 | Yes                   |
|                   | MAJCOM                               |                       |

<sup>\*</sup>FCI candidates will require EP study; all others will require Holter monitor and treadmill testing.

AIMWITS search in Jan 2018 revealed 237 waivers submitted for WPW pattern on ECG, WPW syndrome, or other pre-excitation syndrome. Of the total, 27 were FC I/IA cases, 90 were FC II, 91 were FC III, 4 were RPA only, 3 were MOD, and 22 were ATC or GBC. A total of 29 cases were disqualified. Of the 27 disqualified cases, 5 were FC I, 5 were FC II, 16 were FC III, and 3 were ATC/GBC. Of the total of 29 disqualified cases, 14 were due to insufficient treatment/non-approved medication or failed therapy, 12 for other medical problems, 2 were for not having enough time after treatment for stability prior to waiver submission, and in 1 of the cases it was unknown.

# II. Information Required for Waiver Submission.

The aeromedical summary (AMS) should only be submitted after clinical disposition has been completed and all appropriate treatments have been initiated using best current clinical guidelines/recommendations.

The AMS for the initial waiver for WPW should include the following:

- A. List and fully discuss all clinical diagnoses requiring a waiver.
- B. A complete discussion of the history of WPW as well as any treatments.
- C. Consultation from a cardiologist.
- D. Studies: ECG demonstrating WPW and any other ECGs, Exercise Treadmill Test, Holter monitor, Echocardiography with video, any electrophysiologic studies or therapy. Include video and imaging whenever possible.

Note 1: All studies should be submitted electronically to the EKG Library. To expedite the case, recommend sending via FedEx. Include patient's name, SSN and POC at base.

The address to send videotape/CD and reports not attached in AIMWTS is:

Attn: Case Manager for (patient's MAJCOM) USAFSAM/FECI Facility 20840 2510 Fifth Street WPAFB, OH 45433-7913

Note 2: State in AMS when studies were sent to ACS.

The AMS for waiver renewal for WPW should include the following:

A. Interval history with any change in symptoms, medications or activity level.

B. ECG

C. Any new applicable cardiac studies if done (see Note 1 above).

#### III. Overview.

Wolff-Parkinson-White (WPW) is the well-known abnormal cardiac conduction pattern defined by an accessory electrical pathway that bypasses the atrioventricular node (AVN). WPW pattern is the electrocardiographic pattern of ventricular pre-excitation where the ECG usually demonstrates a shortened PR interval (less than 0.12 seconds) and a prolonged QRS complex (> 0.12 seconds) that demonstrates a slow rising onset of the QRS complex, or fusion, often referred to as a delta wave.<sup>1,2</sup> WPW Pattern is the presence of electrical evidence of accessory pathway on EKG in the absence of any evidence consistent with tachydysrhythmias.<sup>1,2</sup> However, WPW Syndrome requires both electrical evidence of accessory pathway and evidence of tachydysrhythmia. Prevalence of WPW pattern identified by EKG has been estimated to be 0.1 to 3.1 per 1000 persons in the general population.<sup>1, 3, 4</sup> WPW pattern, once identified on EKG may not be a permanent finding as the accessory pathway may conduct slowly, intermittently, or only retrograde and thus be termed a "concealed pathway," which likely leads to an underestimate of the true prevalence. 3, 5, 6, 7 In a study of aviators with known WPW syndrome, there was still only an incidence of dysrhythmias of 1 percent per patient year. This finding was supported by a meta-analysis of asymptomatic preexcitation in 2012 that showed the risk of sudden cardiac death that varied from 0.35 to 1.25 per 1000 person years of follow up and the risk of developing SVT was 16 per 1000 person years of follow up. 10 Most recently the USAF published the largest study in asymptomatic aircrew with WPW pattern that demonstrated a prevalence of 0.3% with an annual rate of arrhythmia of 0.95% and risk of sudden cardiac death of 0.03% per year over 10 years. Those at highest risk were younger, with lower blood pressure, lower total cholesterol, and higher physical fitness testing scores.<sup>7</sup>

Recommendations by the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in 2015 suggest the usefulness of electrophysiologic (EP) studies of both symptomatic and asymptomatic persons with WPW pattern on EKG. While other modalities of determining high risk v/s low risk potential of preexcitation have some utility, an EP study is the most effective at identifying high risk characteristics of accessory pathways. The effectiveness and risks of treatment of high risk accessory pathways was radiofrequency (RF) ablation was reviewed in a systematic review in conjunction with the

ACC/AHA/HRS guidelines.<sup>12</sup> This review showed the complication rate of RF ablation to be between 0.9% and 1% of cases (these included ablation induced right bundle branch block, complete heart block, access site complications, and pneumothorax). In five years of follow-up, those that underwent RF ablation had a 7% incidence of arrhythmic events and those who did not undergo ablation had an incidence of 77%. Due to the success rate of RF ablation in high-risk accessory pathways and low incidence of complications, this is the preferred treatment modality.

While most cases of WPW are sporadic, there is a familial tendency in about 3.4% of all cases. Studies have shown that this is from a mutation in the <u>PR</u>otein <u>Kinase</u>, <u>AMP-activated</u>, <u>Gamma 2</u> non-catalytic subunit (PRKAG2) gene. In familial WPW there is a higher risk of multiple accessory pathways and high risk pathways. Routine genetic testing for WPW is not currently recommended.

## IV. Aeromedical Concerns.

Aeromedical concerns involve risk of recurrent arrhythmia and symptoms that may incapacitate the aviator or otherwise adversely affect flying performance. WPW syndrome poses a risk of aberrant electrical conduction that may lead to sustained supraventricular tachycardias, atrial fibrillation, or other dysrhythmia that rarely progresses to ventricular tachycardia or fibrillation and sudden cardiac death (SCD). It is therefore important to identify those aviation candidates who have a high risk of arrhythmia or SCD in order to provide proper treatment and/or disposition. During EP studies, high risk findings include fast conduction over the accessory pathway (often referred to as a short refractory period), multiple pathways, and/or the ability to conduct retrograde (thus allowing for reentry tachycardias). If the WPW pattern resolves with increased heart rates, it is commonly assumed that the pathway cannot conduct quickly. However, this does not rule out the possibilities of retrograde conduction or the presence of multiple pathways, which require an EP study. The systematic review, in conjunction with the ACC/AHA/HRS guidelines, showed that the occurrence of arrhythmias in untreated asymptomatic individuals in the general population could be as high as 77% over five years. The most current Guidelines for management of adult patients with supraventricular

Tachycardia gives a class IIA recommendation for all patients with asymptomatic WPW pattern to undergo EP study to risk-stratify arrhythmic events and treatment with catheter ablation if the EP study identifies high risk; however, they also give a IIA recommendation for observation without further evaluation. Most importantly, the same guideline gives a IIA recommendation to treat with ablation in "asymptomatic patients if the presence of pre-excitation precludes specific employment (such as with pilots)." There were no data from high risk occupations such as pilots presented to support this last recommendation and the most recent study we published demonstrated a less than 1% annual risk of SVT and less than 0.03% risk of SCD; these risks were highest in the youngest and healthiest aircrew. We therefore reserve EP study for those at high risk (any symptoms, arrhythmia, and persistent pre-excitation with exercise) or young age (most initial applicants).

The minimum acceptable diagnostic work up in airmen with WPW pattern is exercise stress testing and a Holter monitor free of high-risk findings. All high-risk findings need an EP study for evaluation and possible treatment. Additionally, pilot candidates may have somewhat increased lifetime risk given younger age and longer duration of possible service therefore, an EP study is recommended in ALL untrained pilot candidates and ablation is recommended if the EP study

reveals any high risk pathway. See ablation waiver guide for more detail regarding waiver after ablation.

| ICD-9 codes for WPW |                                       |
|---------------------|---------------------------------------|
| 426                 | Conduction disorders                  |
| 426.7               | Anomalous atrioventricular excitation |

| ICD-10 codes for WPW |                                      |
|----------------------|--------------------------------------|
| I45.89               | Other specified conduction disorders |
| I45.6                | Pre-excitation syndrome              |

### V. References.

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- 8. Chiu S-N, Wang J-K, Wu M-H, et al. Cardiac Conduction Disturbance Detected in a Pediatric Population. J Pediatr, 2008; 152(1): 85–89.
- 9. Fitzsimmons PJ, McWhirter PD, Peterson DW, and Kruyer WB. The natural history of Wolff-Parkinson-White syndrome in 228 military aviators: A long-term follow-up of 22 years. Am Heart J, 2001; 142(3): 530–36.
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- 11. Al-Khatib SM, Arshad A, Balk EM, et al. Risk Stratification for Arrhythmic Events in Patients With Asymptomatic Pre-Excitation: A Systematic Review for the 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation, 2016; 133(14): e575-e586.
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